Integrated Summary of Safety of

Other Novavax Recombinant Nanoparticle Vaccine Antigens

with Matrix-M1™ Adjuvant

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Compliance Statement

The studies described within were conducted in compliance with an approved clinical study protocol, Good Clinical Practice (GCP) as outlined by ICH E6(R2), and all applicable local and national regulatory requirements. All Essential Documents as defined in ICH E6(R2), Section 8 have been archived in accordance with GCP.

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Integrated Summary of Safety of Other Novavax Recombinant Nanoparticle Vaccine Antigens with Matrix-M1™ Adjuvant

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
AESI	Adverse event of special interest
COVID-19	Coronavirus disease 2019
EBOV GP	Ebolavirus glycoprotein
HA	Hemagglutinin
HIV	Human immunodeficiency virus
IM	Intramuscular
MAAE	Medically attended adverse event
NVX-CoV2373	Severe acute respiratory syndrome coronavirus 2 recombinant spike protein nanoparticle vaccine with Matrix-M1 adjuvant
PT	Preferred term
Quad-NIV	Recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine
r	Recombinant
RSV F	Respiratory syncytial virus fusion protein
S	Spike (protein)
SAE	Serious adverse event
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SARS-CoV-2 rS	Severe acute respiratory syndrome coronavirus 2 recombinant spike protein nanoparticle vaccine
SNMC	Significant new medical condition
SOC	System organ class
SY	Subject-years
TEAE	Treatment-emergent adverse event
Tri-NIV	Recombinant trivalent hemagglutinin nanoparticle influenza vaccine
VRBPAC	Vaccines and Related Biological Products Advisory Committee
USA	United States of America
WHO	World Health Organization

1 INTRODUCTION

1.1 Overall Safety Evaluation Plan

Novavax, Inc. (hereafter referred to as Novavax) is developing its severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) recombinant (r) spike (S) protein nanoparticle vaccine (SARS-CoV-2 rS) with Matrix-M1™ adjuvant (also referred to as NVX-CoV2373) for the active immunization for the prevention of mild, moderate, and severe coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 infection in adults 18 years of age and older. Clinical trials supporting the SARS-CoV-2 rS with Matrix-M1 adjuvant clinical development program are summarized in Table 1. Available data from each of these trials will be provided in individual interim reports; no integrated summary of safety data from the SARS-CoV-2 rS with Matrix-M1 adjuvant studies is available at this time given the urgent need to rapidly prepare data for regulatory submissions during the ongoing global coronavirus pandemic.

To supplement the lack of available long-term safety data (≥ 6 months) in the ongoing clinical trials of SARS-CoV-2 rS with Matrix-M1 adjuvant (Table 1), an integrated analysis of safety was performed in 2,574 adult participants 18 years of age and older across 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens using the same manufacturing platform technology as SARS-CoV-2 rS administered with the same Matrix-M1 adjuvant with safety follow-up ranging from 6 months to 1 year (Table 2).

Table 1 Clinical Trial Experience with SARS-CoV-2 rS with Matrix-M1 Adjuvant

Study Number (Country)	Study Design	Primary Endpoints	Dosage, Duration, and Dosage Regimen	Planned (Treated) Number of Participants	Study Status[1]
2019nCoV-101 – Part 1 (Australia)	Phase 1, randomized, observer-blinded, placebo-controlled in healthy adults 18 to 59 years of age	Safety Immunogenicity	Dose 1/Dose 2 (Days 0, 21)[2] A: Placebo/ Placebo B: 25 µg+0 µg/ 25 µg+0 µg C: 5 µg+50 µg/ 5 µg+50 µg D: 25 µg+50 µg/ 25 µg+50 µg E: 25 µg+50 µg/ Placebo IM injection on Days 0 and 21; antigen and adjuvant were administered as a bedside mixture	A: 25 (23) B: 25 (25) C: 28 (29) D: 28 (28) E: 25 (26)	Ongoing (enrollment complete); Day 189 interim analysis complete
2019nCoV-101 – Part 2 (Australia and US)	Phase 2, randomized, observer-blinded, placebo-controlled in healthy adult participants ≥ 18 to < 85 years of age	Immunogenicity Safety	Dose 1/Dose 2 (Days 0, 21)[2] A: Placebo/ Placebo B: 5 µg+50 µg/ 5 µg+50 µg C: 5 µg+50 µg/ Placebo D: 25 µg+50 µg/ 25 µg+50 µg E: 25 µg+50 µg/ Placebo Dose 3 (Day 189) A: Placebo B1: Placebo B2: 5 µg+50 µg C1: Placebo C2: 5 µg+50 µg D: Placebo E: Placebo IM injection on Days 0, 21, and 189; antigen and adjuvant were administered as a co-formulation	Dose 1/Dose 2 A: 150-300 (255) B: 150-300 (258) C: 150-300 (256) D: 150-300 (259) E: 150-300 (255) Dose 3 A: 300 (0) B1: 150 (0) B2: 150 (0) C1: 150 (0) C2 150 (0) D: 300 (0) E: 300 (0)	Ongoing (enrollment complete); Day 35 interim analysis complete

Table 1 Clinical Trial Experience with SARS-CoV-2 rS with Matrix-M1 Adjuvant

Study Number (Country)	Study Design	Primary Endpoints	Dosage, Duration, and Dosage Regimen	Planned (Treated) Number of Participants	Study Status[1]
2019nCoV-501 (South Africa)	Phase 2a/2b, randomized, observer-blinded, placebo-controlled in healthy adult HIV-negative participants and in medically stable adult HIV-positive participants 18 to 84 years of age	Efficacy Immunogenicity Safety	Placebo 5 µg SARS-CoV-2 rS vaccine + 50 µg Matrix-M1 adjuvant IM injection on Days 0 and 21; antigen and adjuvant were administered as a co-formulation	SARS-CoV-2 rS: 1480-2082 (2211) Placebo: 1480-2082 (2197)	Ongoing (enrollment complete); primary efficacy and safety analysis complete
2019nCoV-302 (UK)	A Phase 3, randomized, observer-blinded, placebo-controlled trial to evaluate the efficacy and safety in adults 18 to 84 years	Efficacy Immunogenicity Safety	Placebo 5 µg SARS-CoV-2 rS vaccine + 50 µg Matrix-M1 adjuvant IM injection on Days 0 and 21; antigen and adjuvant were administered as a co-formulation	SARS-CoV-2 rS: 7500 (7569) Placebo: 7500 (7570)	Ongoing (enrollment complete); primary efficacy and safety analysis complete
2019nCoV-301 (US, Mexico)	A Phase 3, randomized, observer-blinded, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity in adults ≥ 18 years of age	Efficacy Immunogenicity Safety	Placebo 5 µg SARS-CoV-2 rS vaccine + 50 µg Matrix-M1 adjuvant IM injection on Days 0 and 21; antigen and adjuvant were administered as a co-formulation	30,000 (29,868)	Ongoing (enrollment complete); data remain blinded

Abbreviations: HIV = human immunodeficiency virus; IM = intramuscular; SARS-CoV-2 rS = severe acute respiratory syndrome coronavirus 2 recombinant spike protein nanoparticle vaccine; UK = United Kingdom; US = United States of America.

1. Study status as of 01 April 2021.
2. Dose 1: dose of SARS-CoV-2 rS + dose of Matrix-M1 adjuvant administered on Day 0; Dose 2: dose of SARS-CoV-2 rS + dose of Matrix-M1 adjuvant administered on Day 21.

Table 2 Supportive Clinical Trial Experience of Other Novavax Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Study Number (Country)	Study Design	Primary Endpoints	Dosage, Duration, and Dosage Regimen	Planned (Treated) Number of Participants	Duration of Safety Follow-up[1]	Study Status[2]
EBOV-H-101 (Australia)	Phase 1, randomized, observer-blinded, dose-ranging trial of a recombinant Ebolavirus glycoprotein nanoparticle vaccine with and without Matrix-M1 adjuvant in healthy participants 18 to < 50 years of age	Safety Immunogenicity	EBOV GP + Matrix-M1 adjuvant A: 6.5 µg + 0 µg × 2 B: 6.5 µg + 50 µg × 2 C: 6.5 µg + 50 µg × 1 D: 13 µg + 0 µg × 2 E: 13 µg + 50 µg × 2 F: 13 µg + 50 µg × 1 G: 25 µg + 0 µg × 2 H: 25 µg + 50 µg × 2 J: 25 µg + 50 µg × 1 K: 50 µg + 0 µg × 2 L: 50 µg + 50 µg × 2 M: 50 µg + 50 µg × 1 N: Placebo × 2 IM injections on Day 0 (active) and Day 21 (placebo): (× 1) IM injections on Days 0 and 21 (active): (× 2) Antigen and adjuvant were administered as a bedside mixture	A: 15 (15) B: 15 (15) C: 15 (15) D: 15 (15) E: 15 (15) F: 15 (15) G: 15 (15) H: 15 (15) J: 15 (16) K: 15 (15) L: 15 (16) M: 15 (15) N: 50 (48)	386 days	Complete

Table 2 Supportive Clinical Trial Experience of Other Novavax Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Study Number (Country)	Study Design	Primary Endpoints	Dosage, Duration, and Dosage Regimen	Planned (Treated) Number of Participants	Duration of Safety Follow-up[1]	Study Status[2]
RSV-E-205 (Australia)	Phase 2, randomized, observer-blinded trial of recombinant RSV F nanoparticle vaccine with and without aluminum adjuvant or Matrix-M1 adjuvant in clinically stable 60- through 80-year-old participants	Immunogenicity Safety	RSV F A: 135 µg × 1 RSV F + Aluminum B: 95 µg + 0.3 mg × 1 C: 95 µg + 0.3 mg × 2 D: 120 µg + 0.4 mg ×1 E: 120 µg + 0.4 mg × 2 RSVF + Matrix-M1 adjuvant F: 135 µg + 50 µg × 1 G: 135 µg + 50 µg × 2 H: 65 µg + 50 µg × 1 J: 65 µg + 50 µg × 2 K: 35 µg + 50 µg × 1 L: 35 µg + 50 µg × 2 M: Placebo × 2 IM injections on Day 0 (active) and Day 21 (placebo): (× 1) IM injections on Days 0 and 21 (active): (× 2) Antigen and adjuvant were administered as a bedside mixture	A: 25 (26) B: 25 (26) C: 25 (24) D: 25 (25) E: 25 (24) F: 25 (26) G: 25 (25) H: 25 (25) J: 25 (23) K: 25 (25) L: 25 (25) M: 25 (25)	386 days	Complete

Table 2 Supportive Clinical Trial Experience of Other Novavax Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Study Number (Country)	Study Design	Primary Endpoints	Dosage, Duration, and Dosage Regimen	Planned (Treated) Number of Participants	Duration of Safety Follow-up[1]	Study Status[2]
tNIV-E-101 (US)	Phase 1/2 randomized, observer-blinded, active-controlled trial of recombinant trivalent hemagglutinin nanoparticle influenza vaccine with Matrix-M1 adjuvant in healthy participants ≥ 60 years of age	Safety Immunogenicity	HA dose (µg)/strain: (2017-18 H1N1/H3N2/B) Tri-NIV + Matrix-M1 adjuvant A: 15/15/15 + 50 µg B: 60/60/60 + 50 µg C: Fluzone HD 60/60/60 IM injection on Day 0; antigen and adjuvant were administered as a bedside mixture	A: 110 (109) B: 110 (111) C: 110 (110)	365 days	Complete
qNIV-E-201 (US)	Phase 2, randomized, observer-blinded, active-controlled, dose-finding trial of recombinant quadrivalent hemagglutinin nanoparticle influenza antigen with or without Matrix-M1 adjuvant in clinically stable participants ≥ 65 years of age	Immunogenicity Safety	HA dose [µg]/strain (2018-19 H1N1/H3N2/BV/BY) Quad-NIV A: 60/60/60/60 + 50 µg M1 B: 60/60/60/60 + 50 µg M1 C: 60/60/60/60 + 75 µg M1 D: 60/60/90/90 + 50 µg M1 E: 60/60/60/60 + 0 µg M1 + LV F: 2018-19 Fluzone HD G: 2018-19 Flublok Quadrivalent IM injection on Day 0 (A, B, C, F, G) IM injection on Day 0 (D) + IM injection on Day 28 (LV) Antigen and adjuvant were administered as a bedside mixture for Group A and as a co-formulation for Groups B, C, and D.	A: 155 (157) B: 310 (305) C: 155 (156) D: 135 (132) E: 310 (311) F: 155 (153) G: 155 (151)	183 days	Complete

Table 2 Supportive Clinical Trial Experience of Other Novavax Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Study Number (Country)	Study Design	Primary Endpoints	Dosage, Duration, and Dosage Regimen	Planned (Treated) Number of Participants	Duration of Safety Follow-up[1]	Study Status[2]
qNIV-E-301 (US)	Phase 3, randomized, observer-blinded, active-controlled trial of recombinant quadrivalent hemagglutinin nanoparticle influenza antigen with Matrix-M1 adjuvant in clinically stable participants ≥ 65 years of age	Immunogenicity Safety	HA dose [µg]/strain (2019-20 H1N1/H3N2/BV/BY) A: Quad-NIV + Matrix-M1 adjuvant 60/60/60/60 µg + 75 µg B: 2019-20 Fluzone Quadrivalent 15/15/15/15 µg IM injection on Day 0; antigen and adjuvant were administered as a co-formulation	A: 1325 (1333) B: 1325 (1319)	365 days	Complete

Abbreviations: BV = influenza B strain (Victoria lineage); BY = influenza B strain (Yamagata lineage); co = co-formulated; EBOV GP = Ebolavirus glycoprotein; HA = hemagglutinin; IM = intramuscular; LV = licensed influenza vaccine; mix = bedside mixture; RSV F = respiratory syncytial virus fusion protein; US = United States of America.

1. Duration of safety follow-up available for analysis.
2. Study status as of 01 April 2021.

Note: 2017-18 Northern Hemisphere influenza season: A/Michigan/45/2015 (H1N1), A/HongKong/4801/2014 (H3N2), and B/Brisbane/60/2008; 2018-19 Northern Hemisphere influenza season: A/Michigan/45/2015 (H1N1), A/Singapore/INFIMH-16-0019/2016 (H3N2), B/Colorado/60/2017, and B/Phuket/3073/2013; 2019-20 Northern Hemisphere influenza season: A/Brisbane/02/2018 (H1N1) pdm09, A/Kansas/14/2017 (H3N2), B/Maryland/15/2016 (Victoria lineage), and B/Phuket/3073/2013 (Yamagata lineage).

1.2 Narratives of Supporting Safety Studies Evaluating Other Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

1.2.1 EBOV-H-101

This is a completed Phase 1, randomized, observer-blinded, dose-ranging study conducted by Novavax (11 February 2015 to 19 April 2016) to assess the safety and immunogenicity of varying combinations of a recombinant Ebolavirus glycoprotein (EBOV GP) nanoparticle vaccine with or without Matrix-M1 adjuvant in healthy male and non-pregnant adult participants aged 18 to 49 years in Australia (Study EBOV-H-101). A total of 230 participants were enrolled in 3 stages into 1 of 13 vaccine groups that received 1 or 2 intramuscular (IM) injections of EBOV GP (6.5 to 50 µg) with or without 50 µg Matrix-M1 adjuvant, with antigen and adjuvant administered as bedside mixtures (Table 3). Lot numbers of EBOV GP were NVX14EB01 (14 µg/mL), NVX14EB02 (28 µg/mL), NVX14EB03 (55 µg/mL), and NVX14EB04 (110 µg/mL); the lot number for Matrix-M1 adjuvant was 14-170. Injections were given in a volume of 0.5 mL at a 21-day interval; single-dose active groups received placebo for the second dose. A Safety Monitoring Committee reviewed safety data after each stage and throughout the study. The safety analysis included the 7-day solicited injection site and systemic reactogenicity profile; 35-day all adverse event (AE) profile, including medically attended adverse events (MAAEs), significant new medical conditions (SNMCs), serious adverse events (SAEs), and clinical laboratory safety; and all MAAEs, SAEs, and SNMCs through 1 year post-final dose (ie, Day 384).

Table 3: EBOV-H-101 Study Design

Vaccine Group	Day 0 Vaccination		Day 21 Vaccination		Participants per Group		
	EBOV GP Antigen Dose	Matrix-M1 Adjuvant Dose	EBOV GP Antigen Dose	Matrix-M1 Adjuvant Dose	Stage 1	Stage 2	Stage 3
A	6.5 µg	---	6.5 µg	---	5	5	5
B	6.5 µg	50 µg	6.5 µg	50 µg	5	5	5
C	6.5 µg	50 µg	0 µg	---	5	5	5
D	13 µg	---	13 µg	---	5	5	5
E	13 µg	50 µg	13 µg	50 µg	5	5	5
F	13 µg	50 µg	0 µg	---	5	5	5
G	25 µg	---	25 µg	---	0	5	10
H	25 µg	50 µg	25 µg	50 µg	0	5	10
J	25 µg	50 µg	0 µg	---	0	5	10
K	50 µg	---	50 µg	---	0	5	10
L	50 µg	50 µg	50 µg	50 µg	0	5	10
M	50 µg	50 µg	0 µg	---	0	5	10
N	0 µg	---	0 µg	---	10	15	25
				Total Participants per Stage	**40**	**75**	**115**
				Total Participants	**230**		

Abbreviations: EBOV GP = Ebolavirus glycoprotein; IM = intramuscular.
Note: IM injections (0.5 mL volume) were to be administered in alternating deltoids for each vaccination, beginning with the left deltoid.
Note: 0 µg antigen dose is considered placebo.

Table 4 presents the overall summary of treatment-emergent adverse events (TEAEs) reported through Day 384. EBOV GP with and without Matrix-M1 adjuvant were safe and acceptably well tolerated. No deaths were reported. Nine SAEs were reported in 7 participants (see Appendix 1 for detailed listings of SAEs), with 5 participants receiving the EBOV GP vaccine with Matrix-M1 adjuvant. Two SAEs, 1 case of pericarditis in a participant that received 2 doses of 6.5 µg EBOV GP without adjuvant and 1 case of convulsion in a participant that received 2 doses of 13 µg EBOV GP without adjuvant, were deemed as possibly related to the vaccine by the investigator. However, upon careful review of the participants' medical histories, the sponsor deemed the SAEs as not related to trial vaccine (see Appendix 2 for narratives on these participants). Three participants reported TEAEs considered SNMCs; 1 event each in the placebo (sciatica), unadjuvanted (major depression), and adjuvanted (anxiety disorder and major depression) groups. One participant that received 1 dose of the vaccine with adjuvant (Group C) reported psoriasis, an adverse event of special interest (AESI). However, on further investigation, the participant had an ongoing history of psoriasis antedating exposure; therefore, the AESI was not considered related to the trial vaccine.

Table 5 and Table 6, respectively, summarize the proportion of participants with solicited local and systemic TEAEs reported 7 days post-vaccination 1 and 2 by vaccine group. Solicited TEAEs occurred at a higher frequency in the active vaccine groups than in the placebo group and were highest in the two-dose EBOV GP with Matrix-M1 adjuvant groups. Participants in the two-dose EBOV GP with Matrix-M1 adjuvant groups also reported higher frequencies of severe solicited TEAEs post-Dose 2. In contrast, proportions of unsolicited TEAEs were evenly distributed across the vaccines groups with no clear dose-response pattern observed among the active vaccine groups or a clear association with any particular active vaccine group compared to the placebo group. There was also no apparent association of any TEAE at the system organ class (SOC) or preferred term (PT) level with the active vaccine alone or when adjuvanted with Matrix-M1 adjuvant.

The two-dose EBOV GP with Matrix-M1 adjuvant groups were associated with higher incidences of solicited TEAEs and increased reactogenicity after the second dose relative to the unadjuvanted vaccine groups, suggestive of an adjuvant effect. While most solicited TEAEs reported across both active vaccine and the placebo groups were mild to moderate in severity, some increases in severe TEAEs were observed following the second dose, mainly among participants that received 2 doses of adjuvanted vaccine (6 out of 8 participants with severe TEAEs post-Dose 2). All severe TEAEs improved or resolved during study conduct. Local TEAEs of pain at the injection site and systemic TEAEs of headache, fatigue, and muscle pain were the most frequently reported solicited events in the active vaccine groups. Pain, swelling, and redness at the injection site, as well as systemic events of fatigue, headache, muscle pain, nausea, joint pain, and chills occurred more frequently after the second vaccine dose relative to the first dose in the two-dose EBOV GP with Matrix-M1 adjuvant groups. Reports of fever were infrequent in the placebo and active vaccine groups, and none was severe.

Table 4: Overall Summary of Solicited and Unsolicited Treatment-Emergent Adverse Events Through Day 384 in the EBOV-H-101 Study – Safety Population

		Two-Dose, Unadjuvanted Vaccine Groups				One-Dose Adjuvanted Vaccine Groups				Two-Dose, Adjuvanted Vaccine Groups			
Group:	**N**	**A**	**D**	**G**	**K**	**C**	**F**	**J**	**M**	**B**	**E**	**H**	**L**
EBOV GP Dose:	**Placebo**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**
Matrix-M1 Dose:	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**
N=	**N = 48**	**N = 15**	**N = 15**	**N = 15**	**N = 15**	**N = 15**	**N = 15**	**N = 16**	**N = 15**	**N = 15**	**N = 15**	**N = 15**	**N = 16**
All TEAEs	42 (87.5)	12 (80.0)	9 (60.0)	12 (80.0)	13 (86.7)	14 (93.3)	14 (93.3)	14 (87.5)	14 (93.3)	14 (93.3)	14 (93.3)	15 (100.0)	15 (93.8)
Solicited TEAEs	23 (47.9)	8 (53.3)	7 (46.7)	7 (46.7)	9 (60.0)	12 (80.0)	13 (86.7)	11 (68.8)	9 (60.0)	13 (86.7)	14 (93.3)	14 (93.3)	15 (93.8)
Severe	1 (2.1)	0	0	0	0	0	0	0	1 (6.7)	0	2 (13.3)	2 (13.3)	2 (12.5)
Local	5 (10.4)	0	4 (26.7)	3 (20.0)	6 (40.0)	10 (66.7)	12 (80.0)	10 (62.5)	5 (33.3)	13 (86.7)	14 (93.3)	14 (93.3)	15 (93.8)
Systemic	23 (47.9)	8 (53.3)	6 (40.0)	7 (46.7)	5 (33.3)	9 (60.0)	11 (73.3)	7 (43.8)	5 (33.3)	12 (80.0)	11 (73.3)	12 (80.0)	14 (87.5)
Unsolicited TEAEs	37 (77.1)	9 (60.0)	7 (46.7)	8 (53.3)	10 (66.7)	11 (73.3)	13 (86.7)	11 (68.8)	10 (66.7)	12 (80.0)	10 (66.7)	13 (86.7)	10 (62.5)
Related	12 (25.0)	3 (20.0)	3 (20.0)	2 (13.3)	2 (13.3)	4 (26.7)	9 (60.0)	4 (25.0)	5 (33.3)	5 (33.3)	4 (26.7)	7 (46.7)	5 (31.3)
Severe	3 (6.3)	1 (6.7)	1 (6.7)	0	0	2 (13.3)	1 (6.7)	1 (6.3)	1 (6.7)	1 (6.7)	0	2 (13.3)	1 (6.3)
Severe related	1 (2.1)	1 (6.7)	0	0	0	0	0	0	0	0	0	1 (6.7)	0
SAEs	0	1 (6.7)	1 (6.7)	0	0	1 (6.7)	1 (6.7)	1 (6.3)	1 (6.7)	0	1 (6.7)	0	0
Related	0	0	0	0	0	0	0	0	0	0	0	0	0
Deaths	0	0	0	0	0	0	0	0	0	0	0	0	0
SNMCs	1 (2.1)	0	0	0	1 (6.7)	1 (6.7)	0	0	0	0	0	0	0
MAAEs	15 (31.3)	3 (20.0)	4 (26.7)	4 (26.7)	3 (20.0)	5 (33.3)	3 (20.0)	6 (37.5)	5 (33.3)	3 (20.0)	4 (26.7)	4 (26.7)	4 (25.0)

Abbreviations: EBOV GP = Ebolavirus glycoprotein; MAAE = medically attended adverse event; N = number of participants; SAE = serious adverse event; SNMC = significant new medical condition; TEAE = treatment-emergent adverse event.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6 [Dose 1] and from Day 21 to Day 27 [Dose 2]).

Note: Unsolicited TEAEs, SNMCs, MAAEs, and SAEs were reported from an onset date on or after Day 0 through 84 days post-vaccination, and SAEs, SNMCs, MAAEs from post-vaccination on Day 0 through the end of study (Day 384).

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Table 5: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the EBOV-H-101 Study – Safety Population

		Two-Dose, Unadjuvanted Vaccine Groups				One-Dose Adjuvanted Vaccine Groups				Two-Dose, Adjuvanted Vaccine Groups			
Group:	**N**	**A**	**D**	**G**	**K**	**C**	**F**	**J**	**M**	**B**	**E**	**H**	**L**
EBOV GP Dose:	**Placebo**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**
Matrix-M1 Dose:	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**
N1=	**N1 = 48**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**
N2=	**N2 = 47**	**N2 = 14**	**N2 = 13**	**N2 = 13**	**N2 = 15**	**N2 = 15**	**N2 = 14**	**N2 = 16**	**N2 = 15**	**N2 = 14**	**N2 = 15**	**N2 = 15**	**N2 = 15**
Any solicited local TEAE													
Dose 1	4 (8.3)	0	3 (20.0)	2 (13.3)	4 (26.7)	9 (60.0)	11 (73.3)	10 (62.5)	5 (33.3)	9 (60.0)	8 (53.3)	5 (33.3)	11 (68.8)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	3 (6.4)	0	3 (23.1)	1 (7.7)	3 (20.0)	2 (13.3)	2 (14.3)	2 (12.5)	0	13 (92.9)	14 (93.3)	14 (93.3)	14 (93.3)
Severe	0	0	0	0	0	0	0	0	0	0	1 (6.7)	0	2 (13.3)
Pain													
Dose 1	3 (6.3)	0	3 (20.0)	2 (13.3)	4 (26.7)	9 (60.0)	11 (73.3)	10 (62.5)	4 (26.7)	8 (53.3)	6 (40.0)	5 (33.3)	11 (68.8)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	3 (6.4)	0	2 (15.4)	1 (7.7)	3 (20.0)	2 (13.3)	2 (14.3)	2 (12.5)	0	13 (92.9)	14 (93.3)	14 (93.3)	11 (73.3)
Severe	0	0	0	0	0	0	0	0	0	0	1 (6.7)	0	0
Redness													
Dose 1	1 (2.1)	0	0	1 (6.7)	0	2 (13.3)	4 (26.7)	2 (12.5)	1 (6.7)	0	3 (20.0)	1 (6.7)	2 (12.5)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	1 (2.1)	0	1 (7.7)	0	0	0	0	0	0	2 (13.3)	5 (33.3)	6 (40.0)	7 (46.7)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	2 (13.3)
Bruising													
Dose 1	0	0	1 (6.7)	0	1 (6.7)	1 (6.7)	1 (6.7)	0	2 (13.3)	2 (13.3)	3 (20.0)	1 (6.7)	1 (6.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	0	0	0	0	0	0	1 (6.3)	0	0	5 (33.3)	3 (20.0)	1 (6.7)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 5: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the EBOV-H-101 Study – Safety Population

		Two-Dose, Unadjuvanted Vaccine Groups				One-Dose Adjuvanted Vaccine Groups				Two-Dose, Adjuvanted Vaccine Groups			
Group:	**N**	**A**	**D**	**G**	**K**	**C**	**F**	**J**	**M**	**B**	**E**	**H**	**L**
EBOV GP Dose:	**Placebo**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**
Matrix-M1 Dose:	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**
N1=	**N1 = 48**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**
N2=	**N2 = 47**	**N2 = 14**	**N2 = 13**	**N2 = 13**	**N2 = 15**	**N2 = 15**	**N2 = 14**	**N2 = 16**	**N2 = 15**	**N2 = 14**	**N2 = 15**	**N2 = 15**	**N2 = 15**
Swelling													
Dose 1	0	0	0	1 (6.7)	0	1 (6.7)	2 (13.3)	1 (6.3)	2 (13.3)	0	1 (6.7)	1 (6.7)	2 (12.5)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	0	0	0	0	0	0	0	0	6 (42.9)	6 (40.0)	8 (53.3)	5 (33.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	2 (13.3)

Abbreviations: EBOV GP = Ebolavirus glycoprotein; N1 = number of participants who received Dose 1; N2 = number of participants who received Dose 2; TEAE = treatment-emergent adverse event.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6 [Dose 1] and from Day 21 to Day 27 [Dose 2]).

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Table 6: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the EBOV-H-101 Study – Safety Population

		Two-Dose, Unadjuvanted Vaccine Groups				One-Dose Adjuvanted Vaccine Groups				Two-Dose, Adjuvanted Vaccine Groups			
Group:	**N**	**A**	**D**	**G**	**K**	**C**	**F**	**J**	**M**	**B**	**E**	**H**	**L**
EBOV GP Dose:	**Placebo**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**
Matrix-M1 Dose:	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**
N1=	**N1 = 48**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**
N2=	**N2 = 47**	**N2 = 14**	**N2 = 13**	**N2 = 13**	**N2 = 15**	**N2 = 15**	**N2 = 14**	**N2 = 16**	**N2 = 15**	**N2 = 14**	**N2 = 15**	**N2 = 15**	**N2 = 15**
Any solicited systemic TEAE													
Dose 1	21 (43.8)	7 (46.7)	6 (40.0)	5 (33.3)	3 (20.0)	7 (46.7)	11 (73.3)	4 (25.0)	4 (26.7)	10 (66.7)	6 (40.0)	5 (33.3)	7 (43.8)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	12 (25.5)	3 (21.4)	2 (15.4)	4 (30.8)	3 (20.0)	5 (33.3)	4 (28.6)	4 (25.0)	2 (13.3)	9 (64.3)	11 (73.3)	12 (80.0)	12 (80.0)
Severe	1 (2.1)	0	0	0	0	0	0	0	1 (6.7)	0	2 (13.3)	2 (13.3)	0
General systemic events													
Fatigue													
Dose 1	11 (22.9)	4 (26.7)	5 (33.3)	3 (20.0)	1 (6.7)	4 (26.7)	9 (60.0)	2 (12.5)	0	5 (33.3)	5 (33.3)	3 (20.0)	3 (18.8)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	6 (12.8)	2 (14.3)	1 (7.7)	2 (15.4)	1 (6.7)	2 (13.3)	1 (7.1)	3 (18.8)	1 (6.7)	9 (64.3)	7 (46.7)	11 (73.3)	7 (46.7)
Severe	0	0	0	0	0	0	0	0	1 (6.7)	0	1 (6.7)	1 (6.7)	0
Headache													
Dose 1	10 (20.8)	6 (40.0)	2 (13.3)	4 (26.7)	2 (13.3)	4 (26.7)	7 (46.7)	2 (12.5)	1 (6.7)	5 (33.3)	3 (20.0)	4 (26.7)	5 (31.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	7 (14.9)	3 (21.4)	2 (15.4)	2 (15.4)	3 (20.0)	4 (26.7)	2 (14.3)	4 (25.0)	1 (6.7)	9 (64.3)	7 (46.7)	9 (60.0)	8 (53.3)
Severe	0	0	0	0	0	0	0	0	1 (6.7)	0	1 (6.7)	1 (6.7)	0
Muscle pain													
Dose 1	6 (12.5)	2 (13.3)	3 (20.0)	2 (13.3)	1 (6.7)	3 (20.0)	5 (33.3)	2 (12.5)	1 (6.7)	2 (13.3)	2 (13.3)	4 (26.7)	2 (12.5)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	2 (4.3)	1 (7.1)	1 (7.7)	1 (7.7)	1 (6.7)	2 (13.3)	0	2 (12.5)	1 (6.7)	6 (42.9)	8 (53.3)	8 (53.3)	6 (40.0)
Severe	0	0	0	0	0	0	0	0	1 (6.7)	0	2 (13.3)	1 (6.7)	0
Diarrhea													
Dose 1	6 (12.5)	2 (13.3)	2 (13.3)	0	1 (6.7)	2 (13.3)	4 (26.7)	2 (12.5)	2 (13.3)	2 (13.3)	1 (6.7)	1 (6.7)	1 (6.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	3 (6.4)	0	1 (7.7)	2 (15.4)	0	1 (6.7)	1 (7.1)	0	2 (13.3)	1 (7.1)	1 (6.7)	1 (6.7)	0
Severe	1 (2.1)	0	0	0	0	0	0	0	0	0	0	0	0

Table 6: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the EBOV-H-101 Study – Safety Population

		Two-Dose, Unadjuvanted Vaccine Groups				One-Dose Adjuvanted Vaccine Groups				Two-Dose, Adjuvanted Vaccine Groups			
Group:	**N**	**A**	**D**	**G**	**K**	**C**	**F**	**J**	**M**	**B**	**E**	**H**	**L**
EBOV GP Dose:	**Placebo**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**
Matrix-M1 Dose:	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**
N1=	**N1 = 48**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**
N2=	**N2 = 47**	**N2 = 14**	**N2 = 13**	**N2 = 13**	**N2 = 15**	**N2 = 15**	**N2 = 14**	**N2 = 16**	**N2 = 15**	**N2 = 14**	**N2 = 15**	**N2 = 15**	**N2 = 15**
Nausea													
Dose 1	5 (10.4)	0	2 (13.3)	0	0	2 (13.3)	1 (6.7)	1 (6.3)	1 (6.7)	3 (20.0)	0	1 (6.7)	1 (6.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	4 (8.5)	0	0	0	0	0	0	1 (6.3)	2 (13.3)	5 (35.7)	2 (13.3)	6 (40.0)	3 (20.0)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Joint pain													
Dose 1	3 (6.3)	0	1 (6.7)	0	1 (6.7)	1 (6.7)	1 (6.7)	2 (12.5)	0	4 (26.7)	0	1 (6.7)	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	1 (2.1)	0	1 (7.7)	0	1 (6.7)	0	0	1 (6.3)	1 (6.7)	4 (28.6)	3 (20.0)	6 (40.0)	3 (20.0)
Severe	0	0	0	0	0	0	0	0	1 (6.7)	0	1 (6.7)	0	0
Chills													
Dose 1	1 (2.1)	0	3 (20.0)	0	0	1 (6.7)	1 (6.7)	1 (6.3)	1 (6.7)	1 (6.7)	0	1 (6.7)	1 (6.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	2 (4.3)	1 (7.1)	0	0	0	1 (6.7)	0	1 (6.3)	1 (6.7)	3 (21.4)	4 (26.7)	8 (53.3)	5 (33.3)
Severe	1 (2.1)	0	0	0	0	0	0	0	0	0	1 (6.7)	0	0
Vomiting													
Dose 1	1 (2.1)	0	0	0	0	1 (6.7)	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	0	0	0	0	0	0	0	1 (6.7)	0	1 (6.7)	1 (6.7)	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 6: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the EBOV-H-101 Study – Safety Population

		Two-Dose, Unadjuvanted Vaccine Groups				One-Dose Adjuvanted Vaccine Groups				Two-Dose, Adjuvanted Vaccine Groups			
Group:	**N**	**A**	**D**	**G**	**K**	**C**	**F**	**J**	**M**	**B**	**E**	**H**	**L**
EBOV GP Dose:	**Placebo**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**	**6.5 µg**	**13 µg**	**25 µg**	**50 µg**
Matrix-M1 Dose:	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**0 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**	**50 µg**
N1=	**N1 = 48**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 15**	**N1 = 16**
N2=	**N2 = 47**	**N2 = 14**	**N2 = 13**	**N2 = 13**	**N2 = 15**	**N2 = 15**	**N2 = 14**	**N2 = 16**	**N2 = 15**	**N2 = 14**	**N2 = 15**	**N2 = 15**	**N2 = 15**
Fever													
Dose 1	1 (2.1)	0	0	0	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	0	0	0	0	0	0	0	0	0	2 (13.3)	1 (6.7)	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations: EBOV GP = Ebolavirus glycoprotein; N1 = number of participants who received Dose 1; N2 = number of participants who received Dose 2; TEAE = treatment-emergent adverse event.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6 [Dose 1] and from Day 21 to Day 27 [Dose 2]).

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: For Fever: Mild = 38.0 - 38.4°C, Moderate = 38.5 - 38.9°C, Severe = > 38.9°C.

1.2.2 RSV-E-205

This is a completed Phase 2, randomized, observer-blind study conducted by Novavax (16 January 2017 to 24 March 2018) to compare the safety and immunogenicity of varying doses of respiratory syncytial virus fusion protein (RSV F) nanoparticle antigen (ie, 35, 65, 95, 120, and 135 µg) with 50 µg Matrix-M1 adjuvant (bedside mixture) or 0.3 or 0.4 mg aluminum hydroxide adjuvant (co-formulation), or of 135 µg RSV F antigen alone, or placebo, in a 1- or 2-dose regimen on Days 0 and 21 in clinically-stable older male or female adult participants aged 60 to 80 years in Australia (Study RSV-E-205). Antigen and adjuvants were administered at injection volumes ranging from 0.2 to 0.6 mL, depending on the formulation. The lot number for the unadjuvanted RSV F antigen was NVX16RV01 (Groups A, F, G, H, J, K, and L); the lot number for the adjuvanted RSV F vaccine was NVX16RV06 (Groups B, C, D, and E). The lot numbers for Matrix-M1 were M1-102 (Groups H and J) and M1-103 (Groups F, G, K, and L). Up to 25 participants were randomized to 1 of 12 study groups (Table 7). Planned safety assessments included a review of acute (7-day post each dose) solicited TEAEs and all unsolicited TEAEs over 56 days after the first vaccination, as well as MAAEs, SAEs, and SNMCs over 385 days after the first vaccination.

Table 7: RSV-E-205 Study Design

Treatment Group	Participants Per Group	Day 0			Day 21		
		RSV F Antigen Dose	Aluminum Dose	Matrix-M1 Dose	RSV F Antigen Dose	Aluminum Dose	Matrix-M1 Dose
A	25	135 µg	0	0	0	0	0
B	25	95 µg	0.3 mg	0	0	0	0
C	25	95 µg	0.3 mg	0	95 µg	0.3 mg	0
D	25	120 µg	0.4 mg	0	0	0	0
E	25	120 µg	0.4 mg	0	120 µg	0.4 mg	0
F	25	135 µg	0	50 µg	0	0	0
G	25	135 µg	0	50 µg	135 µg	0	50 µg
H	25	65 µg	0	50 µg	0	0	0
J	25	65 µg	0	50 µg	65 µg	0	50 µg
K	25	35 µg	0	50 µg	0	0	0
L	25	35 µg	0	50 µg	35 µg	0	50 µg
M (Placebo)	25	0	0	0	0	0	0

Abbreviation: IM = intramuscular; RSV F = respiratory syncytial virus fusion protein.
Note: The dose volume for all IM injections ranged from 0.2 to 0.6 mL, depending on the formulation. Alternate deltoids were to be used for each vaccination.
Note: Each dose value of antigen and adjuvant was nominal.

Table 8 presents the overall summary of TEAEs reported through Day 385. All formulations of the RSV F nanoparticle vaccine antigen with or without Matrix-M1 adjuvant or the aluminum hydroxide adjuvant were acceptably well tolerated among participants. Two deaths were reported, 1 in the two-dose RSV F 95 µg/0.3 mg aluminum hydroxide adjuvant group (malignant peritoneal neoplasm) and 1 in the placebo group (aortic dissection); both deaths were assessed as

not related to trial vaccine (see Appendix 2 for narrative of deaths). Forty-one (41) SAEs were reported 36 participants in this study (see Appendix 1 for detailed listings of SAEs). None of these SAEs was considered by the investigator to be related to the trial vaccine or placebo. There was no relationship between incidence of SNMCs and MAAEs and receipt of any dose of RSV F with Matrix-M1 adjuvant.

The reported incidences of unsolicited TEAEs were similar across the RSV F with Matrix-M1 adjuvant groups, all of which were higher than in the placebo group. An apparent antigen dose-response effect was seen across the two-dose RSV F with Matrix-M1 adjuvant groups but not across the one-dose RSV F with Matrix-M1 adjuvant groups. Most participants had mild or moderate unsolicited TEAEs, with similar frequencies across the 65 and 135 µg RSV F with Matrix-M1 adjuvant groups (1- and 2-dose groups); these frequencies were higher than in the placebo group. Severe-related unsolicited TEAEs were reported in 3 participants (none of which received Matrix-M1 adjuvant), and no antigen-dose relationship was noted. SAEs and SNMCs occurred in few participants across the RSV F with Matrix-M1 adjuvant groups, and MAAEs occurred at similar frequencies across the RSV F with Matrix-M1 adjuvant and placebo groups.

Solicited TEAEs occurred at higher frequencies in the two-dose RSV F with Matrix-M1 adjuvant groups than in the one-dose RSV F with Matrix-M1 adjuvant groups. This difference was largely driven by solicited local TEAEs and to a lesser extent by solicited systemic TEAEs. No apparent antigen dose-response effects were seen in any of the RSV F with Matrix-M1 adjuvant groups. Most participants had mild or moderate solicited TEAEs, but the frequency of severe events in the two-dose 65 and 135 µg RSV F groups with Matrix-M1 adjuvant were higher than in the one-dose 65 and 135 µg RSV F groups with Matrix-M1 adjuvant, with no apparent antigen dose-response effect.

Table 8: Overall Summary of Solicited and Unsolicited Treatment-Emergent Adverse Events Through Day 385 in the RSV-E-205 Study – Safety Population

	1-Dose, Adjuvanted Vaccine Groups					2-Dose, Adjuvanted Vaccine Groups					1-Dose	
Group:	**B**	**D**	**F**	**H**	**K**	**C**	**E**	**G**	**J**	**L**	**A**	**M**
RSV F Dose:	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**135 µg**	
Adjuvant Dose:	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0 µg**	**Placebo**
Adjuvant:	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**NA**	
N=	**N = 26**	**N = 25**	**N = 26**	**N = 25**	**N = 25**	**N = 24**	**N = 24**	**N = 25**	**N = 23**	**N = 25**	**N = 26**	**N = 25**
All TEAEs	18 (69.2)	22 (88.0)	21 (80.8)	22 (88.0)	21 (84.0)	20 (83.3)	21 (87.5)	25 (100.0)	21 (91.3)	22 (88.0)	23 (88.5)	18 (72.0)
Solicited TEAEs	7 (26.9)	14 (56.0)	12 (46.2)	10 (40.0)	15 (60.0)	12 (50.0)	13 (54.2)	20 (80.0)	16 (69.6)	19 (76.0)	7 (26.9)	9 (36.0)
Severe	1 (3.8)	1 (4.0)	1 (3.8)	0	0	1 (4.2)	2 (8.3)	3 (12.0)	3 (13.0)	0	2 (7.7)	0
Local	2 (7.7)	8 (32.0)	8 (30.8)	7 (28.0)	8 (32.0)	7 (29.2)	11 (45.8)	17 (68.0)	13 (56.5)	17 (68.0)	2 (7.7)	4 (16.0)
Systemic	6 (23.1)	14 (56.0)	8 (30.8)	6 (24.0)	12 (48.0)	10 (41.7)	6 (25.0)	14 (56.0)	14 (60.9)	12 (48.0)	5 (19.2)	9 (36.0)
Unsolicited TEAEs	18 (69.2)	20 (80.0)	20 (76.9)	21 (84.0)	21 (84.0)	19 (79.2)	20 (83.3)	22 (88.0)	19 (82.6)	19 (76.0)	22 (84.6)	17 (68.0)
Related	3 (11.5)	9 (36.0)	2 (7.7)	5 (20.0)	4 (16.0)	2 (8.3)	7 (29.2)	10 (40.0)	7 (30.4)	6 (24.0)	7 (26.9)	3 (12.0)
Severe	3 (11.5)	7 (28.0)	6 (23.1)	9 (36.0)	5 (20.0)	5 (20.8)	5 (20.8)	7 (28.0)	7 (30.4)	4 (16.0)	7 (26.9)	4 (16.0)
Severe/related	1 (3.8)	1 (4.0)	0	0	0	0	0	0	0	0	1 (3.8)	0
SAEs	3 (11.5)	2 (8.0)	2 (7.7)	3 (12.0)	5 (20.0)	2 (8.3)	3 (12.5)	4 (16.0)	4 (17.4)	1 (4.0)	4 (15.4)	3 (12.0)
Related	0	0	0	0	0	0	0	0	0	0	0	0
Deaths	0	0	0	0	0	1 (4.2)	0	0	0	0	0	1 (4.0)
Related	0	0	0	0	0	0	0	0	0	0	0	0
SNMCs	5 (19.2)	2 (8.0)	2 (7.7)	3 (12.0)	3 (12.0)	3 (12.5)	1 (4.2)	1 (4.0)	4 (17.4)	2 (8.0)	6 (23.1)	3 (12.0)
MAAEs	16 (61.5)	14 (56.0)	17 (65.4)	15 (60.0)	14 (56.0)	17 (70.8)	13 (54.2)	9 (36.0)	13 (56.5)	13 (52.0)	18 (69.2)	13 (52.0)

Abbreviations: Alum = aluminum hydroxide; MAAE = medically attended adverse event; Matrix = Matrix-M1; N = number of participants; NA = not applicable; RSV F = respiratory syncytial virus fusion protein; SAE = serious adverse event; SNMC = significant new medical condition; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6 and Day 21 through Day 27).

Note: unsolicited TEAEs, SNMCs, MAAEs, and SAEs with an onset date on or after Day 0 through 21 days post-vaccination, and SAEs, SNMCs, MAAEs from post-vaccination on Day 0 through the end of study (Day 385).

Table 9 and Table 10 present a summary of the local and systemic reactogenicity profile of participants who received the RSV F protein with Matrix-M1 adjuvant or aluminum adjuvant, compared to placebo or unadjuvanted vaccinees within the first 7 days of each dosing (Day 0 and Day 21).

Solicited local TEAEs generally occurred at similar frequencies after Dose 1 in the RSV F with Matrix-M1 adjuvanted groups, all of which were higher than in the placebo group (although not higher in general than in the groups receiving aluminum adjuvant). After Dose 2, solicited local TEAEs occurred more frequently in the two-dose RSV F with Matrix-M1 adjuvant groups than in the one-dose RSV F with Matrix-M1 adjuvant or placebo groups with no antigen dose-response effect. This difference was largely driven by pain and redness. A similar pattern was noted for injection site pain, although not redness, in recipients of 2 doses of aluminum-adjuvanted vaccines. Severe solicited local TEAEs occurred in few participants.

Solicited systemic TEAEs generally occurred at similar frequencies across the RSV F with Matrix-M1 adjuvant and placebo groups after first vaccination. After second vaccination, there were higher frequencies of solicited local TEAEs in the two-dose 65 and 135 µg RSV F with Matrix-M1 adjuvant groups than in the one-dose RSV F with Matrix-M1 adjuvant, aluminum-adjuvant, or placebo groups with no antigen dose-response effect. This difference was largely driven by muscle pain and fatigue. Most solicited systemic TEAEs were mild or moderate in severity, with severe events occurring in few participants.

Table 9: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the RSV-E-205 Study – Safety Population

	1-Dose Adjuvanted Vaccine Groups					2-Dose Adjuvanted Vaccine Groups					1-Dose	
Group:	**B**	**D**	**F**	**H**	**K**	**C**	**E**	**G**	**J**	**L**	**A**	**M**
RSV F Dose:	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**135 µg**	
Adjuvant Dose:	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0 µg**	**Placebo**
Adjuvant:	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**NA**	
N1=	**N1 = 26**	**N1 = 25**	**N1 = 26**	**N1 = 25**	**N1 = 25**	**N1 = 24**	**N1 = 24**	**N1 = 25**	**N1 = 23**	**N1 = 25**	**N1 = 26**	**N1 = 25**
N2=	**N2 = 23**	**N2 = 25**	**N2 = 26**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 25**	**N2 = 22**	**N2 = 25**	**N2 = 25**	**N2 = 23**
Any solicited local TEAE												
Dose 1	2 (7.7)	8 (32.0)	8 (30.8)	7 (28.0)	8 (32.0)	5 (20.8)	6 (25.0)	5 (20.0)	7 (30.4)	10 (40.0)	2 (7.7)	2 (8.0)
Severe	0	0	0	0	0	0	1 (4.2)	1 (4.0)	0	0	0	0
Dose 2	0	3 (12.0)	1 (3.8)	0	0	7 (29.2)	8 (33.3)	14 (56.0)	12 (54.5)	15 (60.0)	0	2 (8.7)
Severe	0	0	0	0	0	0	0	2 (8.0)	0	0	0	0
Pain												
Dose 1	1 (3.8)	7 (28.0)	6 (23.1)	7 (28.0)	5 (20.0)	5 (20.8)	5 (20.8)	5 (20.0)	7 (30.4)	10 (40.0)	2 (7.7)	1 (4.0)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	3 (12.0)	1 (3.8)	0	0	7 (29.2)	7 (29.2)	12 (48.0)	11 (50.0)	10 (40.0)	0	2 (8.7)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Bruising												
Dose 1	1 (3.8)	1 (4.0)	1 (3.8)	0	2 (8.0)	1 (4.2)	0	0	1 (4.3)	2 (8.0)	0	2 (8.0)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	1 (4.0)	0	0	0	0	0	3 (12.0)	2 (9.1)	2 (8.0)	0	1 (4.3)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Redness												
Dose 1	0	0	1 (3.8)	1 (4.0)	2 (8.0)	0	1 (4.2)	1 (4.0)	1 (4.3)	2 (8.0)	0	0
Severe	0	0	0	0	0	0	0	1 (4.0)	0	0	0	0
Dose 2	0	1 (4.0)	0	0	0	1 (4.2)	1 (4.2)	7 (28.0)	5 (22.7)	7 (28.0)	0	0
Severe	0	0	0	0	0	0	0	2 (8.0)	0	0	0	0

Table 9: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the RSV-E-205 Study – Safety Population

	1-Dose Adjuvanted Vaccine Groups					2-Dose Adjuvanted Vaccine Groups					1-Dose	
Group:	**B**	**D**	**F**	**H**	**K**	**C**	**E**	**G**	**J**	**L**	**A**	**M**
RSV F Dose:	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**135 µg**	
Adjuvant Dose:	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0 µg**	**Placebo**
Adjuvant:	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**NA**	
N1=	**N1 = 26**	**N1 = 25**	**N1 = 26**	**N1 = 25**	**N1 = 25**	**N1 = 24**	**N1 = 24**	**N1 = 25**	**N1 = 23**	**N1 = 25**	**N1 = 26**	**N1 = 25**
N2=	**N2 = 23**	**N2 = 25**	**N2 = 26**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 25**	**N2 = 22**	**N2 = 25**	**N2 = 25**	**N2 = 23**
Swelling												
Dose 1	0	2 (8.0)	1 (3.8)	0	3 (2.0)	0	3 (12.5)	1 (4.0)	3 (13.0)	2 (8.0)	0	0
Severe	0	0	0	0	0	0	1 (4.2)	1 (4.0)	0	0	0	0
Dose 2	0	2 (8.0)	0	0	0	1 (4.2)	2 (8.3)	7 (28.0)	3 (13.6)	5 (20.0)	0	0
Severe	0	0	0	0	0	0	0	1 (4.0)	0	0	0	0

Abbreviations: Alum = aluminum hydroxide; Matrix = Matrix-M1; N1 = number of participants who received Dose 1; N2 = number of participants who received Dose 2; RSV F = respiratory syncytial virus fusion protein; TEAE = treatment-emergent adverse event.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6 [Dose 1] and from Day 21 to Day 27 [Dose 2]).

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Table 10: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the RSV-E-205 Study – Safety Population

	1-Dose Adjuvanted Groups					2-Dose Adjuvanted Groups					1-Dose	
Group:	**B**	**D**	**F**	**H**	**K**	**C**	**E**	**G**	**J**	**L**	**A**	**M**
RSV F Dose:	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**135 µg**	
Adjuvant Dose:	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0 µg**	**Placebo**
Adjuvant:	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**NA**	
N1=	**N1 = 26**	**N1 = 25**	**N1 = 26**	**N1 = 25**	**N1 = 25**	**N1 = 24**	**N1 = 24**	**N1 = 25**	**N1 = 23**	**N1 = 25**	**N1 = 26**	**N1 = 25**
N2=	**N2 = 23**	**N2 = 25**	**N2 = 26**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 25**	**N2 = 22**	**N2 = 25**	**N2 = 25**	**N2 = 23**
Any solicited systemic TEAE												
Dose 1	5 (19.2)	12 (48.0)	6 (23.1)	5 (20.0)	10 (40.0)	6 (25.0)	4 (16.7)	6 (24.0)	7 (30.4)	7 (28.0)	5 (19.2)	9 (36.0)
Severe	1 (3.8)	1 (4.0)	1 (3.8)	0	0	1 (4.2)	0	0	1 (4.3)	0	2 (7.7)	0
Dose 2	1 (4.3)	8 (32.0)	3 (11.5)	2 (8.3)	5 (20.8)	6 (25.0)	4 (16.7)	10 (40.0)	12 (54.5)	7 (28.0)	1 (4.0)	3 (13.0)
Severe	0	0	0	0	0	0	1 (4.2)	1 (4.0)	2 (9.1)	0	1 (4.0)	0
Chills												
Dose 1	0	0	2 (7.7)	0	0	0	0	1 (4.0)	0	0	1 (3.8)	0
Severe	0	0	0	0	0	0	0	0	0	0	1 (3.8)	0
Dose 2	0	0	0	0	1 (4.2)	0	1 (4.2)	0	3 (13.6)	1 (4.0)	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Diarrhea												
Dose 1	1 (3.8)	4 (16.0)	1 (3.8)	0	1 (4.0)	3 (12.5)	2 (8.3)	1 (4.0)	3 (13.0)	1 (4.0)	4 (15.4)	4 (16.0)
Severe	0	0	1 (3.8)	0	0	1 (4.2)	0	0	0	0	1 (3.8)	0
Dose 2	0	1 (4.0)	2 (7.7)	0	1 (4.2)	0	2 (8.3)	3 (12.0)	2 (9.1)	0	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Fatigue												
Dose 1	2 (7.7)	3 (12.0)	5 (19.2)	3 (12.0)	4 (16.0)	1 (4.2)	0	2 (8.0)	3 (13.0)	3 (12.0)	2 (7.7)	3 (12.0)
Severe	1 (3.8)	0	1 (3.8)	0	0	0	0	0	1 (4.3)	0	1 (3.8)	0
Dose 2	0	6 (24.0)	2 (7.7)	1 (4.2)	0	4 (16.7)	3 (12.5)	3 (12.0)	7 (31.8)	4 (16.0)	1 (4.0)	1 (4.3)
Severe	0	0	0	0	0	0	1 (4.2)	1 (4.0)	1 (4.5)	0	1 (4.0)	0
Headache												
Dose 1	2 (7.7)	6 (24.0)	3 (11.5)	1 (4.0)	4 (16.0)	2 (8.3)	1 (4.2)	5 (20.0)	3 (13.0)	4 (16.0)	2 (7.7)	7 (28.0)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	1 (4.3)	3 (12.0)	1 (3.8)	1 (4.2)	1 (4.2)	3 (12.5)	2 (8.3)	5 (20.0)	7 (31.8)	3 (12.0)	0	3 (13.0)
Severe	0	0	0	0	0	0	0	0	1 (4.5)	0	0	0

Table 10: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the RSV-E-205 Study – Safety Population

	1-Dose Adjuvanted Groups					2-Dose Adjuvanted Groups					1-Dose	
Group:	**B**	**D**	**F**	**H**	**K**	**C**	**E**	**G**	**J**	**L**	**A**	**M**
RSV F Dose:	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**135 µg**	
Adjuvant Dose:	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0 µg**	**Placebo**
Adjuvant:	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**NA**	
N1=	**N1 = 26**	**N1 = 25**	**N1 = 26**	**N1 = 25**	**N1 = 25**	**N1 = 24**	**N1 = 24**	**N1 = 25**	**N1 = 23**	**N1 = 25**	**N1 = 26**	**N1 = 25**
N2=	**N2 = 23**	**N2 = 25**	**N2 = 26**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 25**	**N2 = 22**	**N2 = 25**	**N2 = 25**	**N2 = 23**
Joint pain												
Dose 1	1 (3.8)	1 (4.0)	2 (7.7)	1 (4.0)	1 (4.0)	1 (4.2)	1 (4.2)	1 (4.0)	2 (8.7)	0	1 (3.8)	1 (4.0)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	1 (4.0)	1 (3.8)	0	0	0	1 (4.2)	3 (12.0)	3 (13.6)	1 (4.0)	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Muscle pain												
Dose 1	1 (3.8)	3 (12.0)	2 (7.7)	4 (16.0)	6 (24.0)	1 (4.2)	0	1 (4.0)	4 (17.4)	0	1 (3.8)	1 (4.0)
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	3 (12.0)	0	0	3 (12.5)	1 (4.2)	1 (4.2)	3 (12.0)	9 (40.9)	4 (16.0)	1 (4.0)	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Nausea												
Dose 1	1 (3.8)	2 (8.0)	1 (3.8)	0	0	1 (4.2)	1 (4.2)	0	2 (8.7)	1 (4.0)	1 (3.8)	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	3 (12.0)	0	0	1 (4.2)	0	3 (12.5)	2 (8.0)	4 (18.2)	1 (4.0)	0	1 (4.3)
Severe	0	0	0	0	0	0	0	0	1 (4.5)	0	0	0
Fever												
Dose 1	0	1 (4.0)	0	0	2 (8.0)	0	0	0	0	0	0	0
Severe	0	1 (4.0)	0	0	0	0	0	0	0	0	0	0
Dose 2	0	0	0	0	0	0	0	0	1 (4.5)	0	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0

Table 10: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the RSV-E-205 Study – Safety Population

	1-Dose Adjuvanted Groups					2-Dose Adjuvanted Groups					1-Dose	
Group:	**B**	**D**	**F**	**H**	**K**	**C**	**E**	**G**	**J**	**L**	**A**	**M**
RSV F Dose:	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**95 µg**	**120 µg**	**135 µg**	**65 µg**	**35 µg**	**135 µg**	
Adjuvant Dose:	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0.3 mg**	**0.4 mg**	**50 µg**	**50 µg**	**50 µg**	**0 µg**	**Placebo**
Adjuvant:	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**Alum**	**Alum**	**Matrix**	**Matrix**	**Matrix**	**NA**	
N1=	**N1 = 26**	**N1 = 25**	**N1 = 26**	**N1 = 25**	**N1 = 25**	**N1 = 24**	**N1 = 24**	**N1 = 25**	**N1 = 23**	**N1 = 25**	**N1 = 26**	**N1 = 25**
N2=	**N2 = 23**	**N2 = 25**	**N2 = 26**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 24**	**N2 = 25**	**N2 = 22**	**N2 = 25**	**N2 = 25**	**N2 = 23**
Vomiting												
Dose 1	0	0	0	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0	0	0	0
Dose 2	0	1 (4.0)	0	0	0	0	0	0	1 (4.5)	1 (4.0)	0	0
Severe	0	0	0	0	0	0	0	0	1 (4.5)	0	0	0

Abbreviations: Alum = aluminum hydroxide; Matrix = Matrix-M1; N1 = number of participants who received Dose 1; N2 = number of participants who received Dose 2; RSV F = respiratory syncytial virus fusion protein; TEAE = treatment-emergent adverse event.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6 [Dose 1] and from Day 21 to Day 27 [Dose 2]).

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: For Fever: Mild = 38.0 - 38.4°C, Moderate = 38.5 - 38.9°C, Severe = > 38.9°C.

1.2.3 tNIV-E-101

This is a completed Phase 1/2, randomized, observer-blinded, active-controlled clinical trial conducted by Novavax (18 September 2017 to 26 October 2018) in 330 healthy participants ≥ 60 years of age (< 20% of participants were ≥ 75 years of age) to determine the safety and immunogenicity of trivalent nanoparticle influenza vaccine (Tri-NIV) with Matrix-M1 adjuvant (Study tNIV-E-101). Participants were randomized into 1 of 3 vaccine groups to receive an IM injection of 15 or 60 µg hemagglutinin (HA) per strain of Tri-NIV with 50 µg Matrix-M1 adjuvant in a 0.3 or 0.8 mL volume, respectively, with antigen and adjuvant administered as bedside mixtures and pre-configured active comparator (Fluzone HD) administered at the manufacturer's recommended dose and volume (Table 11). The lot number of Tri-NIV was NVX17SF01, and the lot number of Matrix-M1 adjuvant was M1-104. The 2017-18 Northern Hemisphere season strains were A/Michigan/45/2015 (H1N1); A/HongKong/4801/2014 (H3N2); and B/Brisbane/60/2008. The safety analysis included the 7-day solicited injection site and systemic reactogenicity profile; all AEs through 21 days post-injection; and MAAEs, SAEs, and SNMCs through 1 year post-Day 0 dosing (Day 364).

Table 11 tNIV-E-101 Study Design

Vaccine Group	Day 0			Day 21	Participants		
	HA Dose/Strain (µg) H1N1/H3N2/B	Total HA Dose (µg)	Matrix-M1 Dose (µg)	Vaccine	Stage 1	Stage 2	Stage 3
Tri-NIV	15 / 15 /15	45	50	LV	20	90	110
Tri-NIV	60 / 60 / 60	180	50	LV	20	90	110
Fluzone HD	60 / 60 / 60	180	0	Placebo	20	90	110
				Total participants	**60**	**270**	**330**

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; HA = hemagglutinin; LV = licensed seasonal influenza vaccine; Tri-NIV = recombinant trivalent hemagglutinin nanoparticle influenza vaccine.
Note: The 2017-18 Northern Hemisphere season strains were A/Michigan/45/2015 (H1N1); A/HongKong/4801/2014 (H3N2); and B/Brisbane/60/2008.

Table 12 presents the overall safety experience through Day 364 of the study. All 3 vaccines were acceptably well tolerated in this older age population. There was 1 death reported in the study. A 60-69-year-old female in the 180 µg Tri-NIV with Matrix-M1 adjuvant group died due to gastric adenocarcinoma, which was assessed as not related to trial vaccine (see Appendix 2 for the narrative of the death). Twenty-seven (27) SAEs occurred in 21 participants, with all SAEs assessed as not related to the trial vaccines (see Appendix 1 for detailed listings of SAEs).

Across the Tri-NIV with Matrix-M1-adjuvant groups, solicited TEAEs occurred at a slightly higher frequency in the high-dose (180 µg) Tri-NIV with Matrix-M1 adjuvant group when contrasted with the low-dose (45 µg) Tri-NIV with Matrix-M1 adjuvant or the Fluzone HD group. This difference was largely driven by solicited local TEAEs, which suggests a potential antigen dose-response effect. Rates of systemic solicited TEAEs were closely similar across all 3 groups. Most solicited TEAEs were mild or moderate in severity, with severe events occurring in few participants. Unsolicited TEAEs occurred at similar frequencies between the 2 Tri-NIV with Matrix-M1 adjuvant dose groups. Most unsolicited TEAEs were mild or moderate in severity, with severe events occurring at a slightly higher frequency in the high-dose antigen

group. SAEs, SNMCs, and MAAEs occurred at similar frequencies across the Tri-NIV with Matrix-M1 adjuvant groups.

Overall, a similar safety profile was seen between the 180 µg Tri-NIV with Matrix-M1 adjuvant and Fluzone HD groups, with the exception of severe solicited TEAEs, which occurred more frequently in the Tri-NIV with Matrix-M1 adjuvant group.

Table 12: Overall Summary of Participants with Treatment-Emergent Adverse Events by Influenza Vaccine Group through Day 364

Adverse Event Category	45 µg Tri-NIV + Matrix-M1 N = 109	180 µg Tri-NIV + Matrix-M1 N = 111	Fluzone HD N = 110
All TEAEs	83 (76.1)	88 (79.3)	83 (75.5)
Solicited TEAEs	30 (27.5)	37 (33.3)	38 (34.5)
Severe	4 (3.7)	4 (3.6)	1 (0.9)
Local	15 (13.8)	26 (23.4)	30 (27.3)
Severe	2 (1.8)	0	1 (0.9)
Systemic	23 (21.1)	24 (21.6)	20 (18.2)
Severe	2 (1.8)	4 (3.6)	0
Unsolicited TEAEs	73 (67.0)	71 (64.0)	71 (64.5)
Related	3 (2.8)	0	3 (2.7)
Severe	4 (3.7)	8 (7.2)	10 (9.1)
Severe/related	0	0	1 (0.9)
SAEs	6 (5.5)	7 (6.3)	8 (7.3)
Related	0	0	0
Deaths	0	1 (0.9)	0
Related	0	0	0
SNMCs	13 (11.9)	10 (9.0)	14 (12.7)
MAAEs	57 (52.3)	59 (53.2)	51 (46.4)

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; MAAE = medically attended adverse event; N, number of participants; SAE = serious adverse event; SNMC = significant new medical condition; TEAE = treatment-emergent adverse event; Tri-NIV = recombinant trivalent hemagglutinin nanoparticle influenza vaccine.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6).

Note: Unsolicited, SNMCs, MAAEs, and SAEs were reported from an onset date on or after Day 0 through 20 days post-vaccination, and SAEs, SNMCs, MAAEs from post-vaccination on Day 0 through the end of study (Day 364).

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Table 13 and Table 14, respectively, presents the solicited local and systemic TEAE profiles through Day 6. Solicited local TEAEs occurred at a higher frequency in the 180 µg Tri-NIV with Matrix-M1 adjuvant group than in the 45 µg Tri-NIV with Matrix-M1 adjuvant group; this difference was largely driven by pain and to a lesser extent by redness. Pain at the injection site was the most frequent solicited local TEAE across all vaccine groups. Severe solicited local TEAEs occurred in 2 participants in the Tri-NIV with Matrix-M1 adjuvant group and

1 participant in the Fluzone HD group. In general, the solicited local TEAE profile of the 180 µg Tri-NIV with Matrix-M1 adjuvant group was similar to the Fluzone HD group. Solicited systemic TEAEs occurred at similar rates across the 3 vaccine groups, with headache and muscle pain being the most frequent. Most solicited systemic TEAEs were mild or moderate in severity, with severe events occurring in few participants but only in the Tri-NIV with Matrix-M1 adjuvant groups.

Table 13: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the tNIV-E-101 Study – Safety Population

Adverse Event Category	45 µg Tri-NIV + Matrix-M1 N = 109	180 µg Tri-NIV + Matrix-M1 N = 111	Fluzone HD N = 110
Any solicited local TEAE	15 (13.8)	26 (23.4)	30 (27.3)
Severe	2 (1.8)	0	1 (0.9)
Pain	11 (10.1)	24 (21.6)	26 (23.6)
Severe	0	0	0
Swelling	6 (5.5)	8 (7.2)	10 (9.1)
Severe	1 (0.9)	0	1 (0.9)
Bruising	3 (2.8)	4 (3.6)	1 (0.9)
Severe	1 (0.9)	0	0
Redness	2 (1.8)	6 (5.4)	0
Severe	0	0	0

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; TEAE = treatment-emergent adverse event; Tri-NIV = recombinant trivalent hemagglutinin nanoparticle influenza vaccine.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Includes solicited TEAEs reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from Day 0 to Day 6).

Table 14: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the tNIV-E-101 Study – Safety Population

Adverse Event Category	45 µg Tri-NIV + Matrix-M1 N = 109	180 µg Tri-NIV + Matrix-M1 N = 111	Fluzone HD N = 110
Any solicited systemic TEAE	23 (21.1)	24 (21.6)	20 (18.2)
Severe	2 (1.8)	4 (3.6)	0
General			
Chills	3 (2.8)	4 (3.6)	4 (3.6)
Severe	0	0	0
Fatigue	6 (5.5)	8 (7.2)	7 (6.4)
Severe	0	1 (0.9)	0
Headache	11 (10.1)	10 (9.0)	6 (5.5)
Severe	0	1 (0.9)	0
Joint Pain	4 (3.7)	4 (3.6)	6 (5.5)
Severe	0	1 (0.9)	0
Muscle Pain	8 (7.3)	10 (9.0)	11 (10.0)
Severe	0	1 (0.9)	0
Oral temperature	1 (0.9)	0	0
Severe	0	0	0
Gastrointestinal			
Diarrhea	6 (5.5)	7 (6.3)	4 (3.6)
Severe	0	1 (0.9)	0
Nausea	2 (1.8)	4 (3.6)	4 (3.6)
Severe	0	0	0
Vomiting	0	1 (0.9)	0
Severe	0	0	0
Respiratory/facial TEAE			
Cough	4 (3.7)	5 (4.5)	5 (4.5)
Severe	1 (0.9)	0	0
Sore throat	4 (3.7)	4 (3.6)	1 (0.9)
Severe	0	0	0
Eye redness	4 (3.7)	1 (0.9)	1 (0.9)
Severe	1 (0.9)	1 (0.9)	0
Hoarseness	1 (0.9)	0	4 (3.6)
Severe	0	0	0

Table 14: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the tNIV-E-101 Study – Safety Population

Adverse Event Category	45 µg Tri-NIV + Matrix-M1 N = 109	180 µg Tri-NIV + Matrix-M1 N = 111	Fluzone HD N = 110
Chest tightness	3 (2.8)	1 (0.9)	1 (0.9)
Severe	0	0	0
Eyelid swelling	1 (0.9)	0	2 (1.8)
Severe	0	0	0
Difficulty breathing	1 (0.9)	0	1 (0.9)
Severe	0	0	0
Wheezing	2 (1.8)	0	0
Severe	0	0	0
Difficulty swallowing	0	0	1 (0.9)
Severe	0	0	0
Facial swelling	1 (0.9)	0	0
Severe	0	0	0

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; TEAE = treatment-emergent adverse event; Tri-NIV = recombinant trivalent hemagglutinin nanoparticle influenza vaccine.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Includes solicited TEAEs reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from trial Day 0 to trial Day 6).

Note: Oral temperature was categorized as: Mild given an oral temperature = 38.0 - 38.4°C, Moderate = 38.5 - 38.9°C, and Severe ≥ 38.9°C.

1.2.4 qNIV-E-201

This is a completed (in reporting phase) Phase 2, randomized, observer-blinded, active-controlled, dose-finding, formulation-optimizing clinical trial of recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine (Quad-NIV) with Matrix-M1 adjuvant conducted by Novavax (24 September 2018 to 16 April 2019) in healthy adult participants ≥ 65 years of age in the USA (Study qNIV-E-201). A total of 1,375 participants was enrolled and randomized into 1 of 7 vaccine groups as shown in Table 15. Randomization was stratified by site and history of receipt of a 2017-18 influenza vaccine. On Day 0, all participants received trial vaccine by IM injection (0.5 mL). Antigen and adjuvant were administered as a bedside mixture for Group A and as a co-formulation in Groups B, C, and D. On Day 28, participants in Group E (unadjuvanted Quad-NIV) received a rescue injection with a 2018-19 licensed seasonal influenza vaccine (Fluzone HD). The lot numbers for the bedside mixture of Quad-NIV and Matrix-M1 adjuvant were WO000425 and WO000416, respectively; the lot numbers for the co-formulations of Quad-NIV with Matrix-M1 adjuvant were WO000422, WO000440, and WO000442 for Groups B, C, and D, respectively. The lot numbers for Fluzone HD and Flublok Quadrivalent were UI981AA and QFAA1801, respectively. All participants in the other groups received an injection of placebo at Day 28 to maintain the trial blind. Trial follow-up for each participant

spanned approximately 6 months from the Day 0 injection. Solicited TEAEs were evaluated from Day 0 through Day 6 and unsolicited TEAEs were evaluated through Day 28, with SAEs, MAAEs, and SNMCs (including AESIs) evaluated through Day 182.

Table 15: qNIV-E-201 Trial Design

Vaccine Group	Day 0 IM Injection				Day 28 IM Injection	Participants			Total
	Vaccine	HA Dose/Strain(µg) (H1N1/H3N2/BV/BY)	Matrix-M1 Adjuvant Dose (µg)	Formulation		Stage 1	Stage 2	Stage 3	
A	Quad-NIV	60, 60, 60, 60	50	In-Clinic Mix	Placebo	20	20	115	155
B		60, 60, 60, 60	50	Co-form	Placebo	20	60	230	310
C		60, 60, 60, 60	75	Co-form	Placebo	20	20	115	155
D		60, 60, 90, 90	50	Co-form	Placebo	0	20	115	135
E		60, 60, 60, 60	0	NA	LV	20	60	230	310
F	2018-19 Fluzone HD (60, 60, 60, 60)				Placebo	20	20	115	155
G	2018-19 Flublok Quadrivalent (45, 45, 45, 45)				Placebo	20	20	115	155
Total participants						120	220	1035	1375

Abbreviations: Bv = B Victoria lineage; BY = B Yamagata lineage; Co-form = co-formulated; Fluzone HD = Fluzone High-Dose Trivalent; HA = hemagglutinin; IM = intramuscular; LV = licensed influenza vaccine; NA = not applicable; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine.

Note: All participants were to receive 2 vaccinations by IM injection in alternating deltoids on Day 0 and Day 28.

Note: Fluzone HD and Flublok Quadrivalent were administered at the manufacturer's recommended dose and volume.

Note: On Day 28, participants in Group E were to receive a rescue injection with a licensed seasonal influenza vaccine (Fluzone HD); all other participants were to receive a placebo injection to maintain trial blind.

Note: Enrollment was divided into 3 stages. Stage 1 enrolled a total of approximately 120 participants (approximately 20 participants per vaccine group, excluding Group D for which no participants were enrolled in Stage 1). Stage 2 enrolled a total of approximately 220 participants (approximately 20 [Groups A, C, D, F, and G] or 60 participants [Groups B and E] per vaccine group). The remainder of the participants (approximately 1,035 participants total, ie, 115 [Groups A, C, D, F, and G] or 230 participants [Groups B and E] per vaccine group) were enrolled in Stage 3.

Note: The 2018-19 Northern Hemisphere season strains were A/Michigan/45/2015 (H1N1), A/Singapore/INFIMH-16-0019/2016 (H3N2), B/Colorado/60/2017, and B/Phuket/3073/2013.

Table 16 presents the overall safety experience of participants through Day 182 in the study. Overall, various formulations (antigen/adjuvant doses) of Quad-NIV administered alone or with Matrix-M1 adjuvant showed an acceptable safety profile and were acceptably well tolerated, with no significant dose-related toxicities observed. A total of 7 participants died during the course of the study, with all events assessed as not related to the trial vaccines; all events occurred at least > 1 month following vaccination on Day 0. The majority of these participants had a significant medical history (eg, cardiac, respiratory) related to their cause of death (see Appendix 2 for narratives of death). A total of 63 SAEs occurred in 59 participants, all of which were assessed as not related to trial vaccine (see Appendix 1 for detailed listings of SAEs). The highest proportion of SAEs occurred in the high-dose Quad-NIV group with Matrix-M1 adjuvant. TEAEs, SNMCs, and MAAEs were similarly distributed across the vaccine groups.

A comparison of same dose Quad-NIV with and without Matrix-M1 adjuvant (vaccine groups B versus E, respectively) generally showed higher frequencies of solicited local and unsolicited TEAEs and slightly higher severe events in the adjuvanted group than in the unadjuvanted group.

There was no apparent Matrix-M1 adjuvant dose-response effect between the 50 µg and 75 µg groups (vaccine groups B versus C, respectively), and no apparent antigen dose-response effect between the 60 µg and 90 µg antigen dose groups (vaccine groups B versus D, respectively) except possibly for SAEs.

Table 17 and Table 18, respectively, presents the solicited local and systemic TEAE profile for participants. Solicited local TEAEs occurred at a higher frequency in the same dose Quad-NIV with Matrix-M1 adjuvant than in the unadjuvanted group (vaccine groups B versus E, respectively), with the difference largely driven by pain. Pain was the most frequent solicited local TEAE across all vaccine groups. There was no apparent Matrix-M1 adjuvant dose-response effect between the 50 µg and 75 µg groups (vaccine groups B versus C, respectively), and no apparent antigen dose-response effect between the 60 µg and 90 µg B virus antigen dose groups (vaccine groups B versus D, respectively). All but 4 events were mild or moderate in severity. Solicited systemic TEAEs occurred at similar frequencies across the Quad-NIV with Matrix-M1 adjuvant and unadjuvanted vaccine groups. The most frequent solicited systemic TEAEs in the Quad-NIV with Matrix-M1 adjuvant groups were muscle pain, headache, and fatigue.

There were similar frequencies of solicited systemic TEAEs across the vaccine groups. No Matrix-M1 adjuvant effect or Matrix-M1 adjuvant dose response was observed.

Table 16: Overall Summary of Solicited and Unsolicited Treatment-Emergent Adverse Events Through Day 182 in the qNIV-E-201 Study – Safety Population

Group	A	B	C	D	E	F	G
HA and Matrix-M1 Adjuvant Content (µg)	**Quad-NIV A60/B60/M50**	**Quad-NIV A60/B60/M50**	**Quad-NIV A60/B60/M75**	**Quad-NIV A90/B90/M50**	**Quad-NIV A60/B60/M0**	**Fluzone HD**	**Flublok Quadrivalent**
Quad-NIV and Matrix-M1 Formulation	**Bed-side**	**Co-formulated**			**NA**	**NA**	**NA**
Adverse Event Category	**N = 157**	**N = 305**	**N = 156**	**N = 132**	**N = 311**	**N = 153**	**N = 151**
All TEAEs	100 (63.7)	189 (62.0)	92 (59.0)	71 (53.8)	100 (63.7)	189 (62.0)	92 (59.0)
Solicited TEAEs	61 (38.9)	99 (32.5)	59 (37.8)	39 (29.5)	85 (27.3)	58 (37.9)	56 (37.1)
Severe	3 (1.9)	10 (3.3)	5 (3.2)	2 (1.5)	4 (1.3)	2 (1.3)	4 (2.6)
Local	30 (19.1)	74 (24.3)	34 (21.8)	22 (16.7)	40 (12.9)	40 (26.1)	22 (14.6)
Severe	1 (0.6)	2 (0.7)	0	0	1 (0.3)	0	0
Systemic	42 (26.8)	63 (20.7)	45 (28.8)	27 (20.5)	65 (20.9)	37 (24.2)	39 (25.8)
Severe	2 (1.3)	9 (3.0)	5 (3.2)	2 (1.5)	3 (1.0)	2 (1.3)	4 (2.6)
Unsolicited TEAEs	73 (46.5)	144 (47.2)	56 (35.9)	52 (39.4)	104 (33.4)	59 (38.6)	56 (37.1)
Related	8 (5.1)	18 (5.9)	5 (3.2)	5 (3.8)	8 (2.6)	7 (4.6)	6 (4.0)
Severe	10 (6.4)	20 (6.6)	11 (7.1)	11 (8.3)	13 (4.2)	6 (3.9)	7 (4.6)
Severe/related	0	1 (0.3)	0	0	0	0	0
SAEs	8 (5.1)	16 (5.2)	8 (5.1)	12 (9.1)	6 (1.9)	6 (3.9)	3 (2.0)
Related	0	0	0	0	0	0	0
Deaths	1 (0.6)	3 (1.0)	0	2 (1.5)	0	0	1 (0.7)
Related	0	0	0	0	0	0	0

Table 16: Overall Summary of Solicited and Unsolicited Treatment-Emergent Adverse Events Through Day 182 in the qNIV-E-201 Study – Safety Population

Group	A	B	C	D	E	F	G
HA and Matrix-M1 Adjuvant Content (µg)	**Quad-NIV A60/B60/M50**	**Quad-NIV A60/B60/M50**	**Quad-NIV A60/B60/M75**	**Quad-NIV A90/B90/M50**	**Quad-NIV A60/B60/M0**	**Fluzone HD**	**Flublok Quadrivalent**
Quad-NIV and Matrix-M1 Formulation	**Bed-side**	**Co-formulated**			**NA**	**NA**	**NA**
Adverse Event Category	**N = 157**	**N = 305**	**N = 156**	**N = 132**	**N = 311**	**N = 153**	**N = 151**
SNMCs	5 (3.2)	18 (5.9)	10 (6.4)	10 (7.6)	15 (4.8)	6 (3.9)	9 (6.0)
MAAEs	51 (32.5)	87 (28.5)	29 (18.6)	38 (28.8)	74 (23.8)	34 (22.2)	40 (26.5)

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; N = number of participants who received trial vaccine at Day 0; MAAE = medically attended adverse event; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; SAE = serious adverse event; SNMC = significant new medical condition; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination 1 window (ie, from Day 0 through Day 6).

Note: Unsolicited TEAEs, SNMCs, MAAEs, and SAEs were reported with an onset date on or after Day 0 to Day 181 post-vaccination.

Table 17: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-201 Study – Safety Population

Vaccine Group	A	B	C	D	E	F	G
HA and Matrix-M1 Adjuvant Content (µg)	**Quad-NIV A60/B60/M50**	**Quad-NIV A60/B60/M50**	**Quad-NIV A60/B60/M75**	**Quad-NIV A90/B90/M50**	**Quad-NIV A60/B60/M0**	**Fluzone HD**	**Flublok Quadrivalent**
Quad-NIV and Matrix-M1 Formulation	**Bed-side**	**Co-formulated**			**NA**	**NA**	**NA**
Solicited Local Adverse Events	**N = 157**	**N = 305**	**N = 156**	**N = 132**	**N = 311**	**N = 153**	**N = 151**
Any solicited local TEAE	30 (19.1)	74 (24.3)	34 (21.8)	22 (16.7)	40 (12.9)	40 (26.1)	22 (14.6)
Severe	1 (0.6)	2 (0.7)	0	0	1 (0.3)	0	0
Bruising	2 (1.3)	11 (3.6)	5 (3.2)	3 (2.3)	6 (1.9)	4 (2.6)	5 (3.3)
Severe	0	0	0	0	0	0	0
Pain	22 (14.0)	59 (19.3)	30 (19.2)	15 (11.4)	32 (10.3)	32 (20.9)	14 (9.3)
Severe	0	0	0	0	0	0	0
Redness	12 (7.6)	21 (6.9)	8 (5.1)	6 (4.5)	11 (3.5)	10 (6.5)	4 (2.6)
Severe	1 (0.6)	0	0	0	1 (0.3)	0	0
Swelling	6 (3.8)	31 (10.2)	11 (7.1)	11 (8.3)	16 (5.1)	12 (7.8)	7 (4.6)
Severe	0	2 (0.7)	0	0	1 (0.3)	0	0

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; N = number of participants who received trial vaccine at Day 0; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Includes solicited TEAEs reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from trial Day 0 to trial Day 6).

Table 18: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-201 Study – Safety Population

Vaccine Group	A	B	C	D	E	F	G
HA and Matrix-M1 Adjuvant Content (µg)	qNIV A60/B60/ M50	qNIV A60/B60/ M50	qNIV A60/B60/ M75	qNIV A90/B90/ M50	qNIV A60/B60/ M0	Fluzone HD	Flublok Quadrivalent
qNIV-Matrix-M1 Formulation	Bed-side	Co-formulated			NA	NA	NA
Solicited systemic adverse events	**N = 157**	**N = 305**	**N = 156**	**N = 132**	**N = 311**	**N = 153**	**N = 151**
Any solicited systemic TEAE	42 (26.8)	63 (20.7)	45 (28.8)	27 (20.5)	65 (20.9)	37 (24.2)	39 (25.8)
Severe	2 (1.3)	9 (3.0)	5 (3.2)	2 (1.5)	3 (1.0)	2 (1.3)	4 (2.6)
Chills	6 (3.8)	10 (3.3)	7 (4.5)	3 (2.3)	8 (2.6)	5 (3.3)	2 (1.3)
Severe	1 (0.6)	0	1 (0.6)	0	0	1 (0.7)	0
Fatigue	17 (10.8)	25 (8.2)	13 (8.3)	10 (7.6)	16 (5.1)	16 (10.5)	10 (6.6)
Severe	0	2 (0.7)	2 (1.3)	0	2 (0.6)	1 (0.7)	1 (0.7)
Headache	16 (10.2)	23 (7.5)	23 (14.7)	13 (9.8)	23 (7.4)	14 (9.2)	14 (9.3)
Severe	0	2 (0.7)	2 (1.3)	1 (0.8)	0	2 (1.3)	3 (2.0)
Joint pain	8 (5.1)	16 (5.2)	12 (7.7)	5 (3.8)	12 (3.9)	12 (7.8)	10 (6.6)
Severe	0	0	1 (0.6)	0	1 (0.3)	1 (0.7)	0
Muscle pain	9 (5.7)	40 (13.1)	16 (10.3)	7 (5.3)	20 (6.4)	22 (14.4)	7 (4.6)
Severe	1 (0.6)	0	1 (0.6)	0	1 (0.3)	1 (0.7)	0
Oral temperature	1 (0.6)	2 (0.7)	2 (1.3)	0	0	0	0
Severe	0	0	0	0	0	0	0
Gastrointestinal systemic TEAEs							
Diarrhea	12 (7.6)	13 (4.3)	9 (5.8)	5 (3.8)	15 (4.8)	6 (3.9)	15 (9.9)
Severe	1 (0.6)	4 (1.3)	1 (0.6)	1 (0.8)	0	0	1 (0.7)
Nausea	5 (3.2)	13 (4.3)	5 (3.2)	0	11 (3.5)	7 (4.6)	3 (2.0)
Severe	0	1 (0.3)	2 (1.3)	0	0	1 (0.7)	0
Vomiting	0	5 (1.6)	1 (0.6)	0	1 (0.3)	1 (0.7)	1 (0.7)
Severe	0	1 (0.3)	1 (0.6)	0	0	1 (0.7)	0

Table 18: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-201 Study – Safety Population

Vaccine Group	A	B	C	D	E	F	G
HA and Matrix-M1 Adjuvant Content (µg)	qNIV A60/B60/ M50	qNIV A60/B60/ M50	qNIV A60/B60/ M75	qNIV A90/B90/ M50	qNIV A60/B60/ M0	Fluzone HD	Flublok Quadrivalent
qNIV-Matrix-M1 Formulation	Bed-side	Co-formulated			NA	NA	NA
Solicited systemic adverse events	N = 157	N = 305	N = 156	N = 132	N = 311	N = 153	N = 151
Respiratory/facial TEAEs							
Chest tightness	1 (0.6)	3 (1.0)	4 (2.6)	5 (3.8)	3 (1.0)	1 (0.7)	2 (1.3)
Severe	0	0	0	0	1 (0.3)	0	0
Cough	11 (7.0)	12 (3.9)	12 (7.7)	5 (3.8)	10 (3.2)	3 (2.0)	8 (5.3)
Severe	0	1 (0.3)	0	0	1 (0.3)	0	1 (0.7)
Difficulty breathing	0	3 (1.0)	3 (1.9)	1 (0.8)	4 (1.3)	3 (2.0)	1 (0.7)
Severe	0	0	0	0	1 (0.3)	0	1 (0.7)
Difficulty swallowing	2 (1.3)	1 (0.3)	4 (2.6)	0	5 (1.6)	1 (0.7)	2 (1.3)
Severe	0	0	0	0	1 (0.3)	0	1 (0.7)
Eye redness	3 (1.9)	1 (0.3)	1 (0.6)	1 (0.8)	6 (1.9)	1 (0.7)	1 (0.7)
Severe	0	0	1 (0.6)	0	0	0	0
Eyelid swelling	2 (1.3)	2 (0.7)	0	0	2 (0.6)	0	0
Severe	0	0	0	0	0	0	0
Facial swelling	0	1 (0.3)	0	0	1 (0.3)	0	0
Severe	0	0	0	0	0	0	0
Hoarseness	5 (3.2)	10 (3.3)	4 (2.6)	1 (0.8)	8 (2.6)	3 (2.0)	1 (0.7)
Severe	0	1 (0.3)	0	0	1 (0.3)	0	0
Sore throat	4 (2.5)	11 (3.6)	12 (7.7)	2 (1.5)	11 (3.5)	6 (3.9)	5 (3.3)
Severe	0	0	2 (1.3)	0	1 (0.3)	0	1 (0.7)

Table 18: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-201 Study – Safety Population

Vaccine Group	A	B	C	D	E	F	G
HA and Matrix-M1 Adjuvant Content (µg)	**qNIV A60/B60/ M50**	**qNIV A60/B60/ M50**	**qNIV A60/B60/ M75**	**qNIV A90/B90/ M50**	**qNIV A60/B60/ M0**	**Fluzone HD**	**Flublok Quadrivalent**
qNIV-Matrix-M1 Formulation	**Bed-side**	**Co-formulated**			**NA**	**NA**	**NA**
Solicited systemic adverse events	**N = 157**	**N = 305**	**N = 156**	**N = 132**	**N = 311**	**N = 153**	**N = 151**
Wheezing	1 (0.6)	3 (1.0)	3 (1.9)	0	3 (1.0)	3 (2.0)	3 (2.0)
Severe	0	0	0	0	1 (0.3)	0	0

Abbreviations: Fluzone HD = Fluzone High-Dose Trivalent; N = number of participants who received trial vaccine at Day 0; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Includes solicited TEAEs reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from trial Day 0 to trial Day 6).

Note: For oral temperature: Mild = 38.0 - 38.4°C, Moderate = 38.5 - 38.9°C, Severe = > 38.9°C.

1.2.5 qNIV-E-301

This is a completed (in reporting phase) Phase 3, randomized, observer-blinded, active-controlled clinical trial conducted by Novavax (14 October 2019 to 29 October 2020) to evaluate the safety of 240 µg Quad-NIV (60 µg HA antigen per influenza strain) co-formulated with 75 µg Matrix-M1 adjuvant and demonstrate immunogenic non-inferiority against a USA-licensed active comparator, Fluzone Quadrivalent, in clinically stable male and female adult participants ≥ 65 years of age (Study qNIV-E-301). Each trial vaccine contained hemagglutinin antigens reflecting the World Health Organization (WHO) and Vaccines and Related Biological Products Advisory Committee (VRBPAC) recommendations for the 2019-2020 Northern Hemisphere influenza season [A/Brisbane/02/2018 (H1N1) pdm09, A/Kansas/14/2017 (H3N2), B/Maryland/15/ 2016 (Victoria lineage), and B/Phuket/3073/2013 (Yamagata lineage). A total of 2,651 participants was enrolled and randomized in a 1:1 ratio into 1 of 2 vaccine groups as shown in Table 19. Randomization was stratified by site, age (65 to < 75 and ≥ 75 years), and history of prior year receipt of the 2018-2019 influenza vaccine. On Day 0, all participants received a single-dose of trial vaccine (Quad-NIV with Matrix-M1 adjuvant or Fluzone Quadrivalent) by IM injection in the nondominant arm, if available for injection. Total injection volumes for Quad-NIV were 0.5 mL. The lot numbers for the co-formulation of Quad-NIV with Matrix-M1 adjuvant and Fluzone Quadrivalent were SC00000037 and UJ247AB, respectively. Fluzone Quadrivalent (15 µg HA antigen per influenza strain) was administered at the manufacturer's recommended dose and volume (0.5 mL). Trial follow-up for each participant spanned approximately 12 months from the Day 0 injection. Solicited TEAEs were evaluated from Day 0 through Day 6 and unsolicited TEAEs were evaluated through Day 28, with MAAEs, and SNMCs evaluated through Day 364.

Table 19: qNIV-E-301 Trial Design

Vaccine Group	Day 0 Trial Vaccine Injection				Site of Injection	Participants Per Group
	Vaccine	Total HA Dose	Matrix-M1 Adjuvant Dose	Injection Volume		
A	Quad-NIV	240 µg	75 µg	0.5 mL	Nondominant arm	1325
B	2019-20 Fluzone Quadrivalent (60 µg total HA dose)					1325
Total trial participants						2650

Abbreviations: HA = hemagglutinin; IM = intramuscular; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine.
Note: HA dose/influenza strain was 60 µg for Quad-NIV and 15 µg for Fluzone Quadrivalent.
Note: Fluzone Quadrivalent was to be administered at the manufacturer's recommended dose and volume.
Note: If the nondominant arm was not available for injection, then the dominant arm was used.

Table 20 presents the overall safety experience through Day 364 of the study. Quad-NIV (240 µg) co-formulated with 75 µg Matrix-M1 adjuvant, relative to Fluzone Quadrivalent, was acceptably well tolerated. Both local and systemic solicited TEAEs occurred more frequently in recipients of the Quad-NIV with Matrix-M1 adjuvant group than in the Fluzone Quadrivalent group. Unsolicited TEAEs, SNMCs, and MAAEs occurred at similar frequencies in both vaccine groups. There were 14 deaths reported through Day 364 of the

study, 7 in each vaccine group; all deaths were assessed as not related to trial vaccine (see Appendix 2 for narratives of deaths). All but 2 deaths occurred > 30 days after vaccination. A 70-79-year-old male in the Quad-NIV with Matrix-M1 adjuvant group died due to decompensated cirrhotic liver disease (prior medical history of cirrhotic liver disease) and cardiac stent collapse (prior medical history of coronary artery disease); liver disease was noted on the same day as vaccination and cardiac stent collapse was noted 4 days after vaccination. A 70-79-year-old female in the Fluzone Quadrivalent group died due to small cell lung cancer, 19 days after vaccination. A total of 137 SAEs occurred in 81 participants in the Quad-NIV group and 126 SAEs occurred in 78 participants in the Fluzone Quadrivalent group, with all SAEs assessed as not related to trial vaccine (see Appendix 1 for detailed listings of SAEs).

Table 20: Overall Summary of Solicited and Unsolicited Treatment-Emergent Adverse Events Through Day 364 in the qNIV-E-301 Study – Safety Population

Adverse Event Category	Quad-NIV with Matrix-M1 Adjuvant N = 1333	Fluzone Quadrivalent N = 1319
All TEAEs	783 (58.7)	697 (52.8)
Solicited TEAEs	551 (41.3)	420 (31.8)
Severe	21 (1.6)	13 (1.0)
Local	372 (27.9)	243 (18.4)
Severe	8 (0.6)	2 (0.2)
Systemic	369 (27.7)	292 (22.1)
Severe	15 (1.1)	11 (0.8)
Unsolicited TEAEs	469 (35.2)	466 (35.3)
Related	65 (4.9)	33 (2.5)
Severe	75 (5.6)	59 (4.5)
Severe/related	10 (0.8)	2 (0.2)
SAEs	81 (6.1)	78 (5.9)
Related	0	0
Deaths	7 (0.5)	7 (0.5)
Related	0	0
SNMCs	42 (3.2)	49 (3.7)
MAAEs	353 (26.5)	354 (26.8)

Abbreviations: N = number of participants who received trial vaccine at Day 0; MAAE = medically attended adverse event; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; SAE = serious adverse event; SNMC = significant new medical condition; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Solicited TEAEs were reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination 1 window (ie, from Day 0 through Day 6).

Note: Unsolicited TEAEs, SNMCs, MAAEs, and SAEs were reported with an onset date on or after Day 0 to Day 364 post-vaccination.

Table 21 and Table 22, respectively, presents the solicited local and systemic TEAE profile for participants. There was a higher frequency of solicited local TEAEs in the Quad-NIV with Matrix-M1 adjuvant group than in the Fluzone Quadrivalent group; this difference was largely driven by injection site pain, although smaller differences were seen for the other solicited local TEAEs. Although few participants had severe solicited local TEAEs, there was a higher frequency of severe solicited TEAEs in the Quad-NIV with Matrix-M1 adjuvant group than in the Fluzone Quadrivalent group.

There was also a higher frequency of solicited general systemic TEAEs in the Quad-NIV with Matrix-M1 adjuvant group than in the Fluzone Quadrivalent group; this difference, albeit small, occurred across all the solicited general systemic TEAEs, but not in the other solicited systemic TEAEs (ie, gastrointestinal and respiratory/facial solicited events).

Table 21: Summary of All and Severe Solicited Local (Injection Site) Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-301 Study – Safety Population

Solicited Adverse Event Category	Quad-NIV with Matrix-M1 Adjuvant N = 1333	Fluzone Quadrivalent N = 1319
Any solicited local TEAE	372 (27.9)	243 (18.4)
Severe	8 (0.6)	2 (0.2)
Bruising	38 (2.9)	29 (2.2)
Severe	1 (0.1)	2 (0.2)
Pain	341 (25.6)	212 (16.1)
Severe	3 (0.2)	0
Redness	67 (5.0)	34 (2.6)
Severe	3 (0.2)	0
Swelling	84 (6.3)	41 (3.1)
Severe	4 (0.3)	0

Abbreviations: N = number of participants who received trial vaccine at Day 0; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Includes solicited TEAEs reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from trial Day 0 to trial Day 6).

Table 22: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-301 Study – Safety Population

Solicited Adverse Event Category	Quad-NIV with Matrix-M1 Adjuvant N = 1333	Fluzone Quadrivalent N = 1319
Any solicited systemic TEAE	372 (27.9)	243 (18.4)
Severe	8 (0.6)	2 (0.2)
Chills	66 (5.0)	44 (3.3)
Severe	5 (0.4)	0
Fatigue	125 (9.4)	93 (7.1)
Severe	5 (0.4)	3 (0.2)
Headache	142 (10.7)	104 (7.9)
Severe	3 (0.2)	2 (0.2)
Joint pain	77 (5.8)	47 (3.6)
Severe	4 (0.3)	0
Muscle pain	167 (12.5)	106 (8.0)
Severe	7 (0.5)	1 (0.1)
Oral temperature	5 (0.4)	4 (0.3)
Severe	0	0
Gastrointestinal systemic TEAEs		
Diarrhea	51 (3.8)	58 (4.4)
Severe	2 (0.2)	2 (0.2)
Nausea	35 (2.6)	23 (1.7)
Severe	1 (0.1)	1 (0.1)
Vomiting	12 (0.9)	9 (0.7)
Severe	0	0
Respiratory/facial TEAEs		
Chest tightness	10 (0.8)	13 (1.0)
Severe	1 (0.1)	0
Cough	65 (4.9)	56 (4.2)
Severe	3 (0.2)	3 (0.2)
Difficulty breathing	13 (1.0)	13 (1.0)
Severe	0	0
Difficulty swallowing	7 (0.5)	14 (1.1)
Severe	0	0
Eye redness	13 (1.0)	18 (1.4)
Severe	0	2 (0.2)

Table 22: Summary of All and Severe Solicited Systemic Treatment-Emergent Adverse Events Through the Solicitation Period in the qNIV-E-301 Study – Safety Population

Solicited Adverse Event Category	Quad-NIV with Matrix-M1 Adjuvant N = 1333	Fluzone Quadrivalent N = 1319
Eyelid swelling	4 (0.3)	8 (0.6)
Severe	0	0
Facial swelling	3 (0.2)	3 (0.2)
Severe	0	0
Hoarseness	29 (2.2)	21 (1.6)
Severe	1 (0.1)	1 (0.1)
Sore throat	42 (3.2)	42 (3.2)
Severe	2 (0.2)	2 (0.2)
Wheezing	17 (1.3)	17 (1.3)
Severe	0	1 (0.1)

Abbreviations: N = number of participants who received trial vaccine at Day 0; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; TEAE = treatment-emergent adverse event.

Note: Data shown are the participant counts and percentages with the TEAEs shown by vaccine group. Percentages are based on the number of participants in each vaccine group who received vaccine on Day 0. Participants with multiple occurrences of the same event are counted once for that event at the greatest severity reported.

Note: Includes solicited TEAEs reported by participants (via diary or spontaneously) with a recorded start date within the 7-day post-vaccination window (ie, from trial Day 0 to trial Day 6).

Note: For oral temperature: Mild = 38.0 - 38.4°C, Moderate = 38.5 - 38.9°C, Severe = > 38.9°C.

2 POOLING STRATEGY

The 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant investigated 4 unique vaccine antigens (EBOV GP, RSV F, Tri-NIV, and Quad-NIV) in both younger and older adult populations. Clinical trials with RSV F, Tri-NIV, and Quad-NIV were designed in older adult participants ≥ 60 years of age, and the clinical trial with EBOV GP was designed in younger adult participants 18 to 49 years of age. Moreover, clinical trials with EBOV GP and RSV F were conducted in Australia and evaluated both one- and two-dose regimens of vaccine antigen (6.5 µg to 135 µg) with Matrix-M1 adjuvant (50 µg) and clinical trials with Tri-NIV and Quad-NIV were conducted in the USA and evaluated one-dose regimens of vaccine antigen (45 µg to 300 µg) with Matrix-M1 adjuvant (50 µg to 75 µg). Based on these differences in clinical trial design and conduct, only SAE and AESI data were pooled across the studies for the integrated analysis of safety and presented by age cohort (18 to 64 years of age and ≥ 65 years of age). AESIs specific to potential immune-mediated medical conditions (PIMMCs) (see list in Table 23) were analyzed across the clinical trials based on the theoretical concern for the development of autoimmune diseases after vaccination with new vaccines containing novel adjuvants. The list is not intended to be exhaustive, nor does it exclude the possibility that other diagnoses may be AESI.

Table 23 Potential Immune-Mediated Medical Conditions

Categories	Diagnoses (as MedDRA Preferred Terms)
Neuroinflammatory disorders:	Acute disseminated encephalomyelitis (including site-specific variants: eg, non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculomyelitis), cranial nerve disorders including paralyses/paresis (eg, Bell's palsy), generalized convulsion, Guillain-Barre syndrome (including Miller Fisher syndrome and other variants), immune-mediated peripheral neuropathies and plexopathies (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy), myasthenia gravis, multiple sclerosis, narcolepsy, optic neuritis, transverse myelitis, uveitis.
Musculoskeletal and connective tissue disorders:	Antisynthetase syndrome, dermatomyositis, juvenile chronic arthritis (including Still's disease), mixed connective tissue disorder, polymyalgia rheumatic, polymyositis, psoriatic arthropathy, relapsing polychondritis, rheumatoid arthritis, scleroderma (including diffuse systemic form and CREST syndrome), spondyloarthritis (including ankylosing spondylitis, reactive arthritis [Reiter's Syndrome] and undifferentiated spondyloarthritis), systemic lupus erythematosus, systemic sclerosis, Sjogren's syndrome.
Vasculitides:	Large vessels vasculitis (including giant cell arteritis such as Takayasu's arteritis and temporal arteritis), medium sized and/or small vessels vasculitis (including polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg–Strauss syndrome [allergic granulomatous angiitis], Buerger's disease [thromboangiitis obliterans], necrotizing vasculitis and ANCA-positive vasculitis [type unspecified], Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis).

Table 23 Potential Immune-Mediated Medical Conditions

Categories	Diagnoses (as MedDRA Preferred Terms)
Gastrointestinal disorders:	Crohn's disease, celiac disease, ulcerative colitis, ulcerative proctitis.
Hepatic disorders:	Autoimmune hepatitis, autoimmune cholangitis, primary sclerosing cholangitis, primary biliary cirrhosis.
Renal disorders:	Autoimmune glomerulonephritis (including IgA nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis).
Cardiac disorders:	Autoimmune myocarditis/cardiomyopathy.
Skin disorders:	Alopecia areata, psoriasis, vitiligo, Raynaud's phenomenon, erythema nodosum, autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis), cutaneous lupus erythematosus, morphoea, lichen planus, Stevens-Johnson syndrome, Sweet's syndrome.
Hematologic disorders:	Autoimmune hemolytic anemia, autoimmune thrombocytopenia, antiphospholipid syndrome, thrombocytopenia.
Metabolic disorders:	Autoimmune thyroiditis, Grave's or Basedow's disease, new onset Hashimoto thyroiditis, diabetes mellitus type 1, Addison's disease.
Other disorders:	Goodpasture syndrome, idiopathic pulmonary fibrosis, pernicious anemia, sarcoidosis.

Abbreviations: ANCA = anti-neutrophil cytoplasmic antibody; IgA = immunoglobulin A; MedDRA = Medical Dictionary for Regulatory Activities.

Safety analyses of other TEAEs are summarized for each clinical trial, as described in Section 1.2.1 for Study EBOV-H-101, Section 1.2.2 for Study RSV-E-205, Section 1.2.3 for Study tNIV-E-101, Section 1.2.4 for Study qNIV-E-201, and Section 1.2.5 for Study qNIV-E-301.

3 OVERALL EXTENT OF EXPOSURE

A total of 2,574 participants received at least 1 dose of Matrix-M1-adjuvanted vaccines across the 5 Novavax-sponsored trials of other recombinant nanoparticle vaccine antigens produced using the same platform technology as SARS-CoV-2 rS with Matrix-M1 adjuvant, with 496 participants receiving vaccine antigens without Matrix-M1 adjuvant (including those who received vaccine antigens with aluminum hydroxide adjuvant), 1,582 participants receiving active influenza vaccine as a comparator, and 73 participants receiving placebo as a comparator (Table 24). This included 2,303 participants (89.5%) who received a single-dose regimen of Matrix-M1-adjuvanted vaccines and 265 participants (10.3%) who received a two-dose regimen of Matrix-M1-adjuvanted vaccines. Duration of safety follow-up ranged from 183 to 386 days.

Within the Matrix-M1-adjuvanted vaccine group, 1,085 participants received the 50 µg dose of Matrix-M1 adjuvant and 1,489 participants received the 75 µg dose of Matrix-M1 adjuvant.

Total exposure (ie, duration of safety follow-up) of vaccine recipients in the Any Dose Matrix-M1-adjuvanted vaccine, Without Matrix-M1-adjuvanted vaccine, Active Influenza Vaccine Comparator, and placebo groups were 2133.5, 336.77, 1450.45, and 70.99 subject-years (SY) of safety follow-up, respectively (Table 25). Median exposures were 351, 183, 351, and 386 days of safety follow-up, respectively.

Table 24 Exposure of Recombinant Nanoparticle Vaccine Antigens with or without Matrix-M1 Adjuvant by Dose in the Integrated Analysis of Safety Across 5 Novavax-Sponsored Clinical Trials

Novavax Trial	Healthy Status/ Age Range	Vaccine					Comparators		Duration of Safety Follow-up
		Antigen/ Number of Doses	Dose Number	With Matrix-M1		Without Matrix-M1	Active Influenza Vaccine	Placebo	
				50 µg	75 µg				
EBOV-H-101	Healthy/ 18 to 49 years	EBOV GP/ 2 doses (Days 0 and 21)	Dose 1	122	NA	60	NA	48	385 days
			Dose 2	119		55		47	
RSV-E-205	Clinically stable/ 60 to 80 years	RSV F/ 2 doses (Days 0 and 21)	Dose 1	149	NA	125	NA	25	386 days
			Dose 2	146		121		23	
tNIV-E-101	Healthy/ ≥ 60 years	Influenza Hemagglutinin/ 1 dose (Day 0)	Dose 1	220	NA	NA	10	NA	365 days
qNIV-E-201	Healthy/ ≥ 65 years	Influenza Hemagglutinin/ 1 dose (Day 0)	Dose 1	594	156	311	153	NA	183 days
qNIV-E-301	Healthy/ ≥ 65 years	Influenza Hemagglutinin/ 1 dose (Day 0)	Dose 1	NA	1333	NA	1319	NA	365 days
Total participants			**Dose 1**	**1085**	**1489**	**496**	**1582**	**73**	**183 to 386 days**
			Dose 2	**265**	**NA**	**176**	**NA**	**70**	

Abbreviations: EBOV GP = Ebolavirus glycoprotein; NA = not applicable; RSV F = respiratory syncytial virus fusion protein.

Table 25 Exposure of Recombinant Nanoparticle Vaccine Antigens with or without Matrix-M1 Adjuvant by Subject-Years in the Integrated Analysis of Safety Across 5 Novavax-Sponsored Clinical Trials

Novavax Trial	Healthy Status/ Age Range	Vaccine						Comparators	
		Antigen/ Number of Doses	Exposure Parameters	With Matrix-M1			Without Matrix-M1	Active Influenza Vaccine	Placebo
				50 µg	75 µg	Any			
EBOV-H-101	Healthy/ 18 to 49 years	EBOV GP/ 2 doses (Days 0 and 21)	Total (SY)	114.63	NA	114.63	55.46	NA	46.68
			Mean (days)	343.2	NA	343.2	337.6	NA	355.2
			Median (days)	386	NA	386	386	NA	386
RSV-E-205	Clinically stable/ 60 to 80 years	RSV F/ 2 doses (Days 0 and 21)	Total (SY)	155.22	NA	155.22	129.38	NA	24.31
			Mean (days)	380.5	NA	380.5	378.0	NA	355.2
			Median (days)	386	NA	386	386	NA	386
tNIV-E-101	Healthy/ ≥ 60 years	Influenza Hemagglutinin/ 1 dose (Day 0)	Total (SY)	218.33	NA	218.33	NA	108.69	NA
			Mean (days)	362.5	NA	362.5	NA	360.9	NA
			Median (days)	364	NA	364	NA	361	NA
qNIV-E-201	Healthy/ ≥ 65 years	Influenza Hemagglutinin/ 1 dose (Day 0)	Total (SY)	287.96	76.01	363.97	151.93	75.20	NA
			Mean (days)	177.1	178.0	177.2	178.4	179.5	NA
			Median (days)	181	182	181	181	181	NA
qNIV-E-301	Healthy/ ≥ 65 years	Influenza Hemagglutinin/ 1 dose (Day 0)	Total (SY)	NA	1281.33	1281.33	NA	1266.56	NA
			Mean (days)	NA	351.1	351.1	NA	350.7	NA
			Median (days)	NA	352	352	NA	351	NA
Total (SY)				**776.15**	**1357.34**	**2133.49**	**336.77**	**1450.45**	**70.99**
Mean (days)				**261.3**	**332.9**	**302.7**	**248.0**	**334.9**	**355.2**
Median (days)				**185**	**351**	**351**	**183**	**351**	**386**

Abbreviations: EBOV GP = Ebolavirus glycoprotein; NA = not applicable; RSV F = respiratory syncytial virus fusion protein; SY = subject-years.

4 DEMOGRAPHIC AND OTHER CHARACTERISTICS OF STUDY POPULATION

Demographic characteristics of the participants, regardless of age group, in the integrated analysis of safety across the 5 Novovax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant were well balanced across all vaccine groups but not with placebo (Table 26). Median ages of participants in the Any Dose Matrix-M1-adjuvanted vaccine, Without Matrix-M1-adjuvanted vaccine, and Active Influenza Vaccine Comparator groups were approximately 70 years; whereas, the median age of participants in the placebo group was 33 years. This imbalance was due to the use of active influenza vaccine comparator groups (no placebo) in the 3 influenza clinical trials (tNIV-E-101, qNIV-E-201, and qNIV-E-301), two of which contributed the largest number of participants to the analysis (qNIV-E-201 and qNIV-E-301). Across all vaccine and placebo groups, the majority of participants were female, White, and Not of Hispanic or Latino origin.

Table 26: Overall Demographics of Participants Included in the Integrated Analysis of Safety Across Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Parameter	Vaccine Antigen				Active Influenza Vaccine Comparator N = 1582	Placebo N = 73
	Without Matrix-M1 Adjuvant N = 496	50 µg Matrix-M1 N = 1985	75 µg Matrix-M1 N = 1489	Any Dose of Matrix-M1 N = 2574		
Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant, n (%)						
qNIV-E-301	0	0	1333 (89.5)	1333 (51.8)	1319 (83.4)	0
qNIV-E-201	311 (62.7)	594 (54.7)	156 (10.5)	750 (29.1)	153 (9.7)	0
tNIV-E-101	0	220 (20.3)	0	220 (8.5)	110 (7.0)	0
RSV-E-205	125 (25.2)	149 (13.7)	0	149 (5.8)	0	25 (34.2)
EBOV-H-101	60 (12.1)	122 (11.2)	0	122 (4.7)	0	48 (65.8)
Sex, n (%)						
Female	290 (58.5)	631 (58.2)	869 (58.4)	1500 (58.3)	1001 (63.3)	57 (78.1)
Male	206 (41.5)	454 (41.8)	620 (41.6)	1074 (41.7)	581 (36.7)	16 (21.9)
Race, n (%)						
White	448 (90.3)	953 (87.8)	1348 (90.5)	2301 (89.4)	1432 (90.5)	67 (91.8)
Black or African American	29 (5.8)	96 (8.8)	120 (8.1)	216 (8.4)	129 (8.2)	0
Asian	7 (1.4)	18 (1.7)	6 (0.4)	24 (0.9)	13 (0.8)	2 (2.7)
American Indian or Alaska Native	3 (0.6)	2 (0.2)	14 (0.9)	16 (0.6)	3 (0.2)	0
Other	7 (1.4)	13 (1.2)	1 (<0.1)	14 (0.5)	4 (0.3)	4 (5.5)
Native Hawaiian or Other Pacific Islander	2 (0.4)	3 (0.3)	0	3 (0.1)	1 (<0.1)	0

Table 26: Overall Demographics of Participants Included in the Integrated Analysis of Safety Across Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Parameter	Vaccine Antigen				Active Influenza Vaccine Comparator N = 1582	Placebo N = 73
	Without Matrix-M1 Adjuvant N = 496	50 µg Matrix-M1 N = 1085	75 µg Matrix-M1 N = 1489	Any Dose of Matrix-M1 N = 2574		
Ethnicity, n (%)						
Not Hispanic or Latino	488 (98.4)	1060 (97.7)	1418 (95.2)	2478 (96.3)	1510 (95.4)	70 (95.9)
Hispanic or Latino	8 (1.6)	25 (2.3)	71 (4.8)	96 (3.7)	72 (4.6)	3 (4.1)
Age (yr)						
Mean	66.0	66.0	72.5	69.7	72.3	41.1
Standard deviation	15.65	15.07	5.67	11.16	5.80	19.83
Median	69.0	69.0	71.0	71.0	71.0	33.0
Min, max	18-101	18-91	65-96	18-96	60-95	18-77

Abbreviations: max = maximum; Min = minimum.

Demographic characteristics of participants 18 to 64 years of age in the integrated analysis of safety across the Novovax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant varied in terms of age by trial given the different age populations enrolled by the study (see Section 1.2) but were balanced in terms of sex (Table 27). This subgroup analysis excluded 2 trials (qNIV-E-201 and qNIV-E-301) that only enrolled participants ≥ 65 years of age. Median ages of participants 18 to 64 years of age in the Any Dose Matrix-M1-adjuvanted vaccine and Without Matrix-M1-adjuvanted vaccine groups were 45 and 34 years, respectively; whereas, the median ages of participants in the Active Influenza Vaccine Comparator and Placebo groups were 62 and 27 years, respectively. The discrepancies in median age were due to the inclusion of Studies RSV-E-205 and tNIV-E-101, which enrolled participants ≥ 60 years of age and contributed participants at the upper age limit of this analysis. Across all vaccine and placebo groups, the majority of participants 18 to 64 years of age were female, White, and Not of Hispanic or Latino origin.

Table 27: Demographics of Participants 18 to 64 Years of Age Included in the Integrated Analysis of Safety Across Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Parameter	Vaccine Antigen				Active Influenza Vaccine Comparator N = 31	Placebo N = 55
	Without Matrix-M1 Adjuvant N = 99	50 µg Matrix-M1 N = 232	75 µg Matrix-M1 N = 0	Any Dose of Matrix-M1 N = 232		
Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant, n (%)						
EBOV-H-101	60 (60.6)	122 (52.6)	0	122 (52.6)	0	48 (87.3)
tNIV-E-101	0	71 (30.6)	0	71 (30.6)	31 (100)	0
RSV-E-205	39 (39.4)	39 (16.8)	0	39 (16.8)	0	7 (12.7)
qNIV-E-201	0	0	0	0	0	0
qNIV-E-301	0	0	0	0	0	0
Sex, n (%)						
Female	62 (62.6)	142 (61.2)	0	142 (61.2)	22 (71.0)	43 (78.2)
Male	37 (37.4)	90 (38.8)	0	90 (38.8)	9 (29.0)	12 (21.8)
Race, n (%)						
White	89 (89.9)	194 (83.6)	NA	194 (83.6)	24 (77.4)	50 (90.9)
Black or African American	0	14 (6.0)	NA	14 (6.0)	5 (16.1)	0
Asian	3 (3.0)	13 (5.6)	NA	13 (5.6)	1 (3.2)	1 (1.8)
Other	5 (5.1)	8 (3.4)	NA	8 (3.4)	1 (3.2)	4 (7.3)
Native Hawaiian or Other Pacific Islander	2 (2.0)	2 (0.9)	NA	2 (0.9)	0	0
American Indian or Alaska Native	0	1 (0.4)	NA	1 (0.4)	0	0
Ethnicity, n (%)						
Hispanic or Latino	98 (99.0)	228 (98.3)	NA	228 (98.3)	31 (100)	54 (98.2)
Not Hispanic or Latino	1 (1.0)	4 (1.7)	NA	4 (1.7)	0 (0.0)	1 (1.8)
Age (yr)						
Mean	41.2	43.8	NA	43.8	62.3	32.1
Standard deviation	17.94	18.24	NA	18.24	1.37	13.74
Median	34.0	45.0	NA	45.0	62.0	27.0
Min, max	18, 64	18, 64	NA	18, 64	60, 64	18, 64

Abbreviations: max = maximum; Min = minimum; NA = not applicable.

Demographic characteristics of participants ≥ 65 years of age in the integrated analysis of safety across the Novovax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant were more balanced than in the younger cohort (Table 28). This analysis excluded 1 trial (EBOV-H-101), which enrolled participants 18 to 49 years of age. Median ages of participants in the Any Dose Matrix-M1-adjuvanted vaccine, Without Matrix-M1-adjuvanted vaccine, and Active Influenza Vaccine Comparator groups were 71 years, and the median age of participants in the Placebo group was 68.5 years. Across all vaccine and placebo groups, the majority of participants ≥ 65 years of age were female, White, and Not of Hispanic or Latino origin.

Table 28: Demographics of Participants ≥ 65 Years of Age Included in the Integrated Analysis of Safety Across Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Parameter	Vaccine Antigen				Active Influenza Vaccine Comparator N = 1551	Placebo N = 18
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose of Matrix-M1 N = 2342		
Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant, n (%)						
qNIV-E-301	0	0	1333 (89.5)	1333 (56.9)	1319 (85.0)	0
qNIV-E-201	311 (78.3)	594 (69.6)	156 (10.5)	750 (32.0)	153 (9.9)	0
tNIV-E-101	0	149 (17.5)	0	149 (6.4)	79 (5.1)	0
RSV-E-205	86 (21.7)	110 (12.9)	0	110 (4.7)	0	18 (100)
EBOV-H-101	0	0	0	0	0	0
Sex, n (%)						
Female	228 (57.4)	489 (57.3)	869 (58.4)	1358 (58.0)	979 (63.1)	14 (77.8)
Male	169 (42.6)	364 (42.7)	620 (41.6)	984 (42.0)	572 (36.9)	4 (22.2)
Race, n (%)						
White	359 (90.4)	759 (89.0)	1348 (90.5)	2107 (90.0)	1408 (90.8)	17 (94.4)
Black or African American	29 (7.3)	82 (9.6)	120 (8.1)	202 (8.6)	124 (8.0)	0
American Indian or Alaska Native	3 (0.8)	1 (0.1)	14 (0.9)	15 (0.6)	3 (0.2)	0
Asian	4 (1.0)	5 (0.6)	6 (0.4)	11 (0.5)	12 (0.8)	1 (5.6)
Other	2 (0.5)	5 (0.6)	1 (<0.1)	6 (0.3)	3 (0.2)	0
Native Hawaiian or Other Pacific Islander	0	1 (0.1)	0	1 (<0.1)	1 (<0.1)	0
Ethnicity, n (%)						
Not Hispanic or Latino	390 (98.2)	832 (97.5)	1418 (95.2)	2250 (96.1)	1479 (95.4)	16 (88.9)
Hispanic or Latino	7 (1.8)	21 (2.5)	71 (4.8)	92 (3.9)	72 (4.6)	2 (11.1)

Table 28: Demographics of Participants ≥ 65 Years of Age Included in the Integrated Analysis of Safety Across Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Parameter	Vaccine Antigen				Active Influenza Vaccine Comparator N = 1551	Placebo N = 18
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose of Matrix-M1 N = 2342		
Age (yr)						
Mean	72.1	72.0	72.5	72.3	72.5	68.5
Standard deviation	5.89	5.39	5.67	5.57	5.68	3.13
Median	71.0	71.0	71.0	71.0	71.0	68.5
Min, max	65, 101	65, 91	65, 96	65, 96	65, 95	65, 77

Abbreviations: max = maximum; Min = minimum; NA = not applicable.

All 5 Novovax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant enrolled healthy or clinically stable adult participants, with no clinically significant underlying medical conditions. Therefore, age was the only relevant baseline characteristic across the trial populations.

5 INTEGRATED ANALYSIS OF ADVERSE EVENTS

5.1 Common Adverse Events

The most common adverse events associated with each of the recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant are solicited local and systemic TEAEs, all of which were assessed within 7 days after each vaccination. These events were not pooled across the 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant given the uniqueness of 4 of the vaccine antigens (EBOV GP, RSV F, Tri-NIV, and Quad-NIV) and dosing regimens (one versus two doses). Rather, solicited local and systemic TEAEs were summarized for each clinical trial, as described in Section 1.2.1 for Study EBOV-H-101, Section 1.2.2 for Study RSV-E-205, Section 1.2.3 for Study tNIV-E-101, Section 1.2.4 for Study qNIV-E-201, and Section 1.2.5 for Study qNIV-E-301.

In general, frequencies of solicited local and systemic TEAEs were increased in recipients who received Matrix-M1-adjuvanted vaccines (compared to those who received vaccines without Matrix-M1 adjuvant) and in recipients who received two-dose Matrix-M1-adjuvanted vaccine (compared to those who received one-dose Matrix-M1-adjuvanted vaccine). Nonetheless, less than 10% of participants reported solicited severe TEAEs across the two-dose Matrix-M1-adjuvanted vaccine groups (Studies EBOV-H-101 and RSV-E-205) and less than 5% of participants reported solicited severe TEAEs across the one-dose Matrix-M1-adjuvanted vaccine groups (Studies tNIV-E-101, qNIV-E-201, and qNIV-E-301).

- In Study EBOV-H-101, which enrolled younger adults 18 to 49 years of age, the most frequent (incidence > 30%) solicited local and systemic TEAEs after first and second vaccination of 6.5 µg to 50 µg EBOV GP with 50 µg Matrix-M1 adjuvant were local TEAEs of pain, swelling, and redness and systemic TEAEs of headache, fatigue, muscle pain, and chills. The frequencies of these events were higher than those in recipients who received one-dose adjuvanted vaccines or placebo. Solicited severe TEAEs were reported in 6 of 61 participants (9.8%) across the two-dose adjuvanted groups, 1 of 61 participants (1.6%) across the one-dose adjuvanted groups, 0 of 60 participants (0%) across the two-dose unadjuvanted vaccine groups, and 1 of 48 participants (2.1%) in the placebo group.
- In Study RSV-E-205, the most frequent (incidence > 15%) solicited local and systemic TEAEs after first and second vaccination of 35 µg to 135 µg RSV F with 50 µg Matrix-M1 adjuvant were pain (local), headache (systemic), fatigue (systemic), and muscle pain (systemic). The frequencies of these events were higher than those in recipients who received unadjuvanted vaccine or placebo. Solicited severe TEAEs were reported in 6 of 73 participants (8.2%) across the two-dose Matrix-M1-adjuvanted vaccine groups, 1 of 76 participants (1.3%) across the one-dose Matrix-M1-adjuvanted vaccine groups, 2 of 51 participants (3.9%) across the one-dose aluminum hydroxide adjuvanted vaccine groups, 2 of 26 participants (7.7%) in the unadjuvanted vaccine group, and 0 of 25 participants (0%) in the placebo group.

- In Study tNIV-E-101, the most frequent (incidence > 10%) solicited local and systemic TEAEs after single-dose vaccination of 45 µg or 180 µg Quad-NIV with 50 µg Matrix-M1 adjuvant was pain. The frequency of this event, in particular the 180 µg dose, was similar to those who received the active influenza vaccine comparator Fluzone HD. Solicited severe TEAEs were reported in 8 of 220 participants (3.6%) across the Tri-NIV with Matrix-M1 adjuvant groups and in 1 of 110 participants (0.9%) in the Fluzone HD group.
- In Study qNIV-E-201, the most frequent (incidence > 10%) solicited local and systemic TEAEs after single-dose vaccination of 240 µg or 300 µg Quad-NIV with 50 µg or 75 µg Matrix-M1 adjuvant were pain (local), headache (systemic), fatigue (systemic), and muscle pain (systemic). The frequencies of these events were similar to those in recipients who received the active influenza vaccine comparator, Fluzone HD (240 µg of total antigen), but higher than those in recipients who received Flublok Quadrivalent (180 µg of total antigen). Solicited severe TEAEs were reported in 3 of 157 participants (1.9%) in the bedside mixture Quad-NIV with Matrix-M1 adjuvant group, and 17 of 593 (2.9%) participants across the co-formulated Quad-NIV with Matrix-M1 adjuvant groups, 2 of 311 participants (1.3%) in the unadjuvanted Quad-NIV group, and 6 of 204 participants (2.9%) across the Fluzone HD and Flublok Quadrivalent groups.
- In Study qNIV-E-301, the most frequent (incidence > 10%) solicited local and systemic TEAEs after single-dose vaccination of 240 µg Quad-NIV with 75 µg Matrix-M1 adjuvant were pain (local), muscle pain (systemic), and headache (systemic). The frequencies of these events were higher than those in recipients who received the active influenza vaccine comparator Fluzone Quadrivalent (60 µg of total antigen). Solicited severe TEAEs occurred in 21 of 1,333 participants (1.6%) in the Quad-NIV with Matrix-M1 adjuvant group and in 13 of 1,319 participants (1.0%) in the active influenza vaccine comparator Fluzone Quadrivalent.

Frequencies of unsolicited TEAEs were generally similar between the treatment groups evaluating various antigens across a wide dose range (6.5 µg to 300 µg recombinant nanoparticle antigen) with or without Matrix-M1 adjuvant (50 µg or 75 µg), including the active influenza vaccine and placebo comparators. In addition, less than 10% of participants in Studies EBOV-H-101, tNIV-E-101, qNIV-E-201, and qNIV-E-301 reported unsolicited severe TEAEs across the Matrix-M1-adjuvanted vaccine groups and less than 30% of participants in Study RSV-E-205 reported unsolicited severe TEAEs across the Matrix-M1-adjuvanted vaccine groups.

In Study EBOV-H-101, unsolicited TEAEs were reported in 45 of 61 participants (73.8%) across the two-dose adjuvanted groups, 45 of 61 participants (73.8%) across the one-dose adjuvanted groups, 34 of 60 participants (56.7%) across the two-dose unadjuvanted vaccine groups, and 37 of 48 participants (77.1%) in the placebo group. Unsolicited severe TEAEs were reported in 4 of 61 participants (6.6%) across the two-dose adjuvanted groups, 5 of 61 participants (8.2%) across the one-dose

adjuvanted groups, 2 of 60 participants (3.3%) across the two-dose unadjuvanted vaccine groups, and 3 of 48 participants (6.3%) in the placebo group.

- In Study RSV-E-205, unsolicited TEAEs were reported in 60 of 73 participants (82.2%) across the two-dose Matrix-M1-adjuvanted vaccine groups, 62 of 76 participants (81.6%) across the one-dose Matrix-M1-adjuvanted vaccine groups, 38 of 51 participants (74.5%) across the one-dose aluminum hydroxide adjuvanted vaccine groups, 22 of 26 participants (84.6%) in the unadjuvanted vaccine group, and 17 of 25 participants (68.0%) in the placebo group. Unsolicited severe TEAEs were reported in 18 of 73 participants (24.7%) across the two-dose Matrix-M1-adjuvanted vaccine groups, 20 of 76 participants (26.3%) across the one-dose Matrix-M1-adjuvanted vaccine groups, 10 of 51 participants (19.6%) across the one-dose aluminum hydroxide adjuvanted vaccine groups, 7 of 26 participants (26.9%) in the unadjuvanted vaccine group, and 4 of 25 participants (16.0%) in the placebo group.
- In Study tNIV-E-101, unsolicited TEAEs were reported in 144 of 220 participants (65.5%) across the Tri-NIV with Matrix-M1 adjuvant groups and in 71 of 110 participants (64.5%) in the Fluzone HD group. Solicited severe TEAEs were reported in 12 of 220 participants (5.5%) across the Tri-NIV with Matrix-M1 adjuvant groups and in 10 of 110 participants (9.1%) in the Fluzone HD group.
- In Study qNIV-E-201, unsolicited TEAEs were reported in 73 of 157 participants (46.5%) in the bedside mixture Quad-NIV with Matrix-M1 adjuvant group, and 252 of 593 (42.5%) participants across the co-formulated Quad-NIV with Matrix-M1 adjuvant groups, 104 of 311 participants (33.4%) in the unadjuvanted Quad-NIV group, and 115 of 204 participants (56.4%) across the Fluzone HD and Flublok Quadrivalent groups. Unsolicited severe TEAEs were reported in 10 of 157 participants (6.4%) in the bedside mixture Quad-NIV with Matrix-M1 adjuvant group, and 42 of 593 (7.1%) participants across the co-formulated Quad-NIV with Matrix-M1 adjuvant groups, 13 of 311 participants (4.2%) in the unadjuvanted Quad-NIV group, and 13 of 204 participants (6.4%) across the Fluzone HD and Flublok Quadrivalent groups.
- In Study qNIV-E-301, unsolicited TEAEs occurred in 469 of 1,333 participants (35.2%) in the Quad-NIV with Matrix-M1 adjuvant group and in 466 of 1,319 participants (35.3%) in the active influenza vaccine comparator Fluzone Quadrivalent. Unsolicited severe TEAEs occurred in 75 of 1,333 participants (5.6%) in the Quad-NIV with Matrix-M1 adjuvant group and in 59 of 1,319 participants (4.5%) in the active influenza vaccine comparator Fluzone Quadrivalent.

5.2 Deaths

There were a total of 24 deaths (0.5%) in 4,725 participants across the 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant (Table 29). Fourteen deaths (0.5%) occurred in 2,574 participants who received Matrix-M1-adjuvanted vaccines, 8 deaths (0.5%) in 1,582 participants who received active influenza vaccine comparator, 1 death (1.4%) in 73 participants who received placebo comparator, and 1 death (0.2%) in 496 participants who received a recombinant nanoparticle vaccine antigen without Matrix-M1 adjuvant. All reported deaths were assessed as not related to study treatment.

All 24 deaths occurred in participants ≥ 65 years of age and were generally as expected for this age population and consistent with participants' medical histories. There was no apparent pattern in the types of deaths reported across the clinical trials. Safety narratives for the 24 deaths are presented in Appendix 2.

Table 29 Listing of Deaths Across the Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Novavax Trial	Treatment Group	Demographics	Description of Death	Relationship to Study Treatment
RSV-E-205	95 µg RSV F, 0.3 mg aluminum hydroxide adjuvant	70-79-year-old male, PPD	Malignant peritoneal neoplasm	Not related
	Placebo	70-79-year-old female, PPD	Aortic dissection	Not related
tNIV-E-101	180 µg Tri-NIV, 50 µg Matrix-M1 adjuvant	60-69-year-old female, PPD	Adenocarcinoma gastric	Not related
qNIV-E-201	Quad-NIV A60/B60/M50 (bedside mix)	70-79-year-old male, PPD	Respiratory failure	Not related
	Quad-NIV A60/B60/M50 (co-formulated)	60-69-year-old female, PPD	Death (unknown etiology)	Not related
	Quad-NIV A60/B60/M50 (co-formulated)	60-69-year-old female, PPD	Aortic aneurysm rupture	Not related
	Quad-NIV A60/B60/M50 (co-formulated)	80-89-year-old female, PPD	Cerebral arteriosclerosis, dementia Alzheimer's type	Not related
	Quad-NIV A90/B90/M50 (co-formulated)	70-79-year-old male, PPD	Lung cancer metastatic	Not related
	Quad-NIV A90/B90/M50 (co-formulated)	80-89-year-old male, PPD	Small intestinal obstruction, pulmonary embolism	Not related
	Flublok Quadrivalent	60-69-year-old male, PPD	Road traffic accident	Not related
qNIV-E-301	Quad-NIV, 75 µg Matrix-M1 adjuvant	80-89-year-old male, PPD	COVID-19	Not related
	Quad-NIV, 75 µg Matrix-M1 adjuvant	70-79-year-old female, PPD	Death	Not related
	Quad-NIV, 75 µg Matrix-M1 adjuvant	70-79-year-old female, PPD	Death	Not related
	Quad-NIV, 75 µg Matrix-M1 adjuvant	80-89-year-old female, PPD	COVID-19	Not related
	Quad-NIV, 75 µg Matrix-M1 adjuvant	80-89-year-old female, PPD	Thrombosis	Not related
	Quad-NIV, 75 µg Matrix-M1 adjuvant	70-79-year-old male, PPD	Decompensated cirrhotic liver disease, cardiac stent collapse	Not related
	Quad-NIV, 75 µg Matrix-M1 adjuvant	60-69-year-old female, PPD	Cardiac failure congestive	Not related
	Fluzone Quadrivalent	70-79-year-old female, PPD	Gastrointestinal hemorrhage, hepatic cirrhosis, shock hemorrhagic	Not related
	Fluzone Quadrivalent	90 or older-year-old male, PPD	Cardiac failure congestive	Not related

Table 29 Listing of Deaths Across the Novavax-Sponsored Clinical Trials of Other Recombinant Nanoparticle Vaccine Antigens with Matrix-M1 Adjuvant

Novavax Trial	Treatment Group	Demographics	Description of Death	Relationship to Study Treatment
	Fluzone Quadrivalent	70-79-year-old female, PPD	Myocardial infarction	Not related
	Fluzone Quadrivalent	70-79-year-old female, PPD	Small cell lung cancer	Not related
	Fluzone Quadrivalent	80-89-year-old female, PPD	Pneumonia, acute respiratory failure, pulmonary embolism	Not related
	Fluzone Quadrivalent	70-79-year-old male, PPD	Small intestinal obstruction, diverticulitis, pneumonia, sepsis	Not related
	Fluzone Quadrivalent	80-89-year-old female, PPD	Subarachnoid hemorrhage	Not related

Abbreviations: A60 = two 60 µg influenza virus A strains; A90 = one 90 µg influenza virus A strain and one 60 µg influenza virus A strain; B60 = two 60 µg influenza virus B strains; B90 = one 90 µg influenza virus B strain and one 60 µg influenza virus B strain; M50 = 50 µg Matrix-M1 adjuvant; Quad-NIV = recombinant quadrivalent hemagglutinin nanoparticle influenza vaccine; RSV F = respiratory syncytial virus fusion protein; Tri-NIV = recombinant trivalent hemagglutinin nanoparticle influenza vaccine; USA = United States of America.

5.3 Other Serious Adverse Events

5.3.1 Participants 18 to 64 Years of Age

A total of 35 SAEs were reported in participants 18 to 64 years of age across the Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant (Table 30). These events occurred at similar exposure-adjusted rates across the Matrix-M1-adjuvanted vaccine (9.3 events per 100 SY), Matrix-M1-unadjuvanted vaccine (10.4 events per 100 SY), and active influenza vaccine comparator (13.1 events per 100 SY) groups in participants 18 to 64 years of age, all of which had higher exposure-adjusted rates than placebo (0 events per 100 SY).

The highest number of SAEs in participants 18 to 64 years of age occurred in the SOCs of Infections and Infestations and Neoplasms Benign, Malignant and Unspecified (including cysts and polyps), with only 1 event occurring for each preferred term. In fact, all SAEs occurred once for each preferred term in participants 18 to 64 years of age. There was no apparent pattern for the reported SAEs across the vaccine groups.

Two SAEs, 1 case of pericarditis in a participant who received 2 doses of 6.5 µg EBOV GP without adjuvant and 1 case of convulsion in a participant who received 2 doses of 13 µg EBOV GP without adjuvant, were deemed as possibly related to the vaccine by the investigator (Table 31). However, upon careful review of the participants' medical histories, the sponsor deemed the SAEs as not related to trial vaccine (see Appendix 1 under Study EBOV-H-101). Pericarditis was reported in a 30-39-year-old male and convulsion was reported in a 30-39-year-old male (see Appendix 2 for narratives on these participants).

Two SAEs (seizure) were reported as PIMMCs in participants 18 to 64 years of age across the Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant; both seizure events (2.1 events per 100 SY) were reported in the Without Matrix-M1-adjuvanted vaccine group. Narratives of serious PIMMCs are presented in Appendix 2.

Table 30: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants 18 to 64 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 99 n (rate)	50 µg Matrix-M1 N = 232 n (rate)	75 µg Matrix-M1 N = 0 n (rate)	Any Dose of Matrix-M1 N = 232 n (rate)	N = 31 n (rate)	N = 55 n (rate)
Total exposure (SY)	**95.80**	**225.15**	**0**	**225.15**	**30.61**	**54.08**
Mean exposure (days)	**353.4**	**354.5**	**NA**	**354.5**	**360.7**	**359.1**
Median exposure (days)	**386**	**383**	**NA**	**383**	**364**	**386**
Total number of SAEs	**10 (10.4)**	**21 (9.3)**	**NA**	**21 (9.3)**	**4 (13.1)**	**0**
Infections and infestations	**1 (1.0)**	**4 (1.8)**	**NA**	**4 (1.8)**	**0**	**0**
Cellulitis	0	1 (0.4)	NA	1 (0.4)	0	0
Pelvic abscess	0	1 (0.4)	NA	1 (0.4)	0	0
Pneumonia	0	1 (0.4)	NA	1 (0.4)	0	0
Rhinovirus infection	0	1 (0.4)	NA	1 (0.4)	0	0
Sepsis	1 (1.0)	0	NA	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1 (1.0)**	**4 (1.8)**	**NA**	**4 (1.8)**	**1 (3.3)**	**0**
Adenocarcinoma gastric	0	1 (0.4)	NA	1 (0.4)	0	0
Ganglioneuroma	0	1 (0.4)	NA	1 (0.4)	0	0
Metastases to meninges	0	1 (0.4)	NA	1 (0.4)	0	0
Prostate cancer metastatic	0	1 (0.4)	NA	1 (0.4)	0	0
Adenocarcinoma pancreas	0	0	NA	0	1 (3.3)	0
Breast cancer	1 (1.0)	0	NA	0	0	0
Nervous system disorders	**3 (3.1)**	**3 (1.3)**	**NA**	**3 (1.3)**	**0**	**0**
Cerebrovascular accident	0	1 (0.4)	NA	1 (0.4)	0	0
Loss of consciousness	0	1 (0.4)	NA	1 (0.4)	0	0
Syncope	0	1 (0.4)	NA	1 (0.4)	0	0
Convulsion	2 (2.1)	0	NA	0	0	0
Sciatica	1 (1.0)	0	NA	0	0	0

Table 30: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants 18 to 64 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 99 n (rate)	50 µg Matrix-M1 N = 232 n (rate)	75 µg Matrix-M1 N = 0 n (rate)	Any Dose of Matrix-M1 N = 232 n (rate)	N = 31 n (rate)	N = 55 n (rate)
Total exposure (SY)	**95.80**	**225.15**	**0**	**225.15**	**30.61**	**54.08**
Mean exposure (days)	**353.4**	**354.5**	**NA**	**354.5**	**360.7**	**359.1**
Median exposure (days)	**386**	**383**	**NA**	**383**	**364**	**386**
Cardiac disorders	**1 (1.0)**	**2 (0.9)**	**NA**	**2 (0.9)**	**2 (6.5)**	**0**
Acute myocardial infarction	0	1 (0.4)	NA	1 (0.4)	0	0
Atrial fibrillation	0	1 (0.4)	NA	1 (0.4)	2 (6.5)	0
Pericarditis	1 (1.0)	0	NA	0	0	0
Injury, poisoning and procedural complications	**0**	**2 (0.9)**	**NA**	**2 (0.9)**	**1 (3.3)**	**0**
Skin abrasion	0	1 (0.4)	NA	1 (0.4)	0	0
Tooth fracture	0	1 (0.4)	NA	1 (0.4)	0	0
Overdose	0	0	NA	0	1 (3.3)	0
Gastrointestinal disorders	**0**	**1 (0.4)**	**NA**	**1 (0.4)**	**0**	**0**
Haemorrhoids thrombosed	0	1 (0.4)	NA	1 (0.4)	0	0
General disorders and administration site conditions	**0**	**1 (0.4)**	**NA**	**1 (0.4)**	**0**	**0**
Chest discomfort	0	1 (0.4)	NA	1 (0.4)	0	0
Hepatobiliary disorders	0	1 (0.4)	NA	1 (0.4)	0	0
Gallbladder polyp	0	1 (0.4)	NA	1 (0.4)	0	0
Renal and urinary disorders	**1 (1.0)**	**1 (0.4)**	**NA**	**1 (0.4)**	**0**	**0**
Nephrolithiasis	0	1 (0.4)	NA	1 (0.4)	0	0
Bladder neck obstruction	1 (1.0)	0	NA	0	0	0
Respiratory, thoracic and mediastinal disorders	**1 (1.0)**	**1 (0.4)**	**NA**	**1 (0.4)**	**0**	**0**
Chronic obstructive pulmonary disease	0	1 (0.4)	NA	1 (0.4)	0	0
Hypoxia	1 (1.0)	0	NA	0	0	0

Table 30: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants 18 to 64 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 99 n (rate)	50 µg Matrix-M1 N = 232 n (rate)	75 µg Matrix-M1 N = 0 n (rate)	Any Dose of Matrix-M1 N = 232 n (rate)	N = 31 n (rate)	N = 55 n (rate)
Total exposure (SY)	**95.80**	**225.15**	**0**	**225.15**	**30.61**	**54.08**
Mean exposure (days)	**353.4**	**354.5**	**NA**	**354.5**	**360.7**	**359.1**
Median exposure (days)	**386**	**383**	**NA**	**383**	**364**	**386**
Vascular disorders	**0**	**1 (0.4)**	**NA**	**1 (0.4)**	**0**	**0**
Peripheral artery thrombosis	0	1 (0.4)	NA	1 (0.4)	0	0
Investigations	1 (1.0)	0	NA	0	0	0
Cardiac murmur	1 (1.0)	0	NA	0	0	0
Musculoskeletal and connective tissue disorders	**1 (1.0)**	**0**	**NA**	**0**	**0**	**0**
Mixed connective tissue disease	1 (1.0)	0	NA	0	0	0

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; NA = applicable; SAE = serious adverse event; SY = subject-years.

Note: Overall exposure was summarized in total SY. This was calculated as follows: SY = sum of duration of exposure in days (for all participants in each vaccine group)/365.25. Unsolicited adverse events were summarized by frequencies and exposure-adjusted event rates (ERs). ERs per 100 SY were calculated by dividing the total number of participants experiencing the unsolicited adverse event by the sum of all participants' time (in 100 years) of exposure during the vaccine follow-up period. The entire exposure time during the vaccine follow-up period was used.

Table 31: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Treatment-Related Serious Adverse Events in Participants 18 to 64 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator N = 31	Placebo N = 55
	Without Matrix-M1 Adjuvant N = 99	50 µg Matrix-M1 N = 232	75 µg Matrix-M1 N = 0	Any Dose Matrix-M1 N = 232		
Total exposure (SY)	**95.80**	**225.15**	**0**	**225.15**	**30.61**	**54.08**
Mean exposure (days)	**353.4**	**354.5**	**0**	**354.5**	**360.7**	**359.1**
Median exposure (days)	**386**	**383**	**0**	**383**	**364**	**386**
Treatment-related SAEs	**2 (2.1)**	**0**	**0**	**0**	**0**	**0**
Cardiac disorders	**1 (1.0)**	**0**	**0**	**0**	**0**	**0**
Pericarditis	1 (1.0)	0	0	0	0	0
Nervous system disorders	**1 (1.0)**	**0**	**0**	**0**	**0**	**0**
Convulsion	1 (1.0)	0	0	0	0	0

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; SY = subject-years.

Note: Overall exposure was summarized in total SY. This was calculated as follows: SY = sum of duration of exposure in days (for all participants in each vaccine group)/365.25. Unsolicited adverse events were summarized by frequencies and exposure-adjusted event rates (ERs). ERs per 100 SY were calculated by dividing the total number of participants experiencing the unsolicited adverse event by the sum of all participants' time (in 100 years) of exposure during the vaccine follow-up period. The entire exposure time during the vaccine follow-up period was used.

Note: Both events were deemed as possibly related to the vaccine by the investigator. However, upon careful review of the participants' medical histories, the sponsor deemed the SAEs as not related to trial vaccine.

5.3.2 Participants ≥ 65 Years of Age

A total of 410 SAEs were reported in participants ≥ 65 years of age across the Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant (Table 32). These events occurred at similar exposure-adjusted rates across the Any Dose Matrix-M1-adjuvanted vaccine (12.6 events per 100 SY), Without Matrix-M1-adjuvanted vaccine (11.6 events per 100 SY), and Active Influenza Vaccine Comparator (9.8 events per 100 SY) groups in participants ≥ 65 years of age, all of which had lower exposure-adjusted rates than Placebo (17.7 events per 100 SY). In the Any Dose Matrix-M1-adjuvanted vaccine group, the exposure-adjusted rates of SAEs were slightly higher in the 50 µg dose group (15.8 events per 100 SY) than in the 75 µg dose group (11.3 events per 100 SY) in participants ≥ 65 years of age.

The highest number of SAEs in participants ≥ 65 years of age occurred in the SOC of Infections and Infestations, with similar exposure-adjusted rates across the Any Dose Matrix-M1-adjuvanted vaccine (3.0 events per 100 SY), Without Matrix-M1-adjuvanted vaccine (2.1 events per 100 SY), and Active Influenza Vaccine Comparator (2.2 events per 100 SY) groups but all lower than in the Placebo group (5.9 events per 100 SY), with pneumonia (0.6, 0, 0.5, and 0 events per 100 SY, respectively), diverticulitis (0.3, 0, 0.1, and 0 events per 100 SY), and sepsis (0.3, 0.4, 0.1, and 0 events per 100 SY) being the most frequent (incidence ≥ 0.3 events per 100 SY). Other frequent SAEs in participants ≥ 65 years of age were cerebrovascular accident (0.3, 0, 0, and 0 events per 100 SY), cardiac failure congestive (0.3, 0.3, 0, and 0 events per 100 SY), respiratory failure (0.3, 0, 0.1, and 0 events per 100 SY), and hepatobiliary disorders (0.3, 0, 0.1, and 0 events per 100 SY).

All SAEs in participants ≥ 65 years of age were assessed as not related to study treatment.

Two SAEs (seizure) were reported as PIMMCs in participants ≥ 65 years of age across the Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant; both seizure events (0.4 subject years) occurred in the 50 µg Matrix-M1-adjuvanted vaccine group.

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Total number of SAEs	**28 (11.6)**	**87 (15.8)**	**153 (11.3)**	**240 (12.6)**	**139 (9.8)**	**3 (17.7)**
Infections and infestations	**5 (2.1)**	**14 (2.5)**	**43 (3.2)**	**57 (3.0)**	**31 (2.2)**	**1 (5.9)**
Pneumonia	0	1 (0.2)	10 (0.7)	11 (0.6)	7 (0.5)	0
Diverticulitis	0	4 (0.7)	2 (0.1)	6 (0.3)	1 (0.1)	0
Sepsis	1 (0.4)	0	5 (0.4)	5 (0.3)	2 (0.1)	0
Covid-19	0	0	4 (0.3)	4 (0.2)	2 (0.1)	0
Influenza	1 (0.4)	3 (0.5)	1 (0.1)	4 (0.2)	1 (0.1)	0
Localised infection	0	0	3 (0.2)	3 (0.2)	0	0
Appendicitis	0	1 (0.2)	1 (0.1)	2 (0.1)	3 (0.2)	0
Cellulitis	2 (0.8)	1 (0.2)	1 (0.1)	2 (0.1)	1 (0.1)	0
Cellulitis staphylococcal	0	0	2 (0.1)	2 (0.1)	0	0
Clostridium difficile infection	0	2 (0.4)	0	2 (0.1)	0	0
Arthritis infective	0	0	1 (0.1)	1 (0.1)	0	0
Bronchitis viral	0	0	1 (0.1)	1 (0.1)	0	0
Covid-19 pneumonia	0	0	1 (0.1)	1 (0.1)	0	0
Gastroenteritis viral	0	0	1 (0.1)	1 (0.1)	0	0
Infected skin ulcer	0	0	1 (0.1)	1 (0.1)	0	0
Lower respiratory tract infection	0	1 (0.2)	0	1 (0.1)	0	0
Osteomyelitis	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Pelvic abscess	0	0	1 (0.1)	1 (0.1)	0	0
Pneumonia bacterial	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant	50 µg Matrix-M1	75 µg Matrix-M1	Any Dose Matrix-M1		
	N = 397	N = 853	N = 1489	N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Septic shock	0	0	1 (0.1)	1 (0.1)	2 (0.1)	0
Staphylococcal bacteraemia	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Staphylococcal infection	0	0	1 (0.1)	1 (0.1)	0	0
Streptococcal bacteraemia	0	0	1 (0.1)	1 (0.1)	0	0
Urinary tract infection	0	1 (0.2)	0	1 (0.1)	1 (0.1)	0
Urosepsis	0	0	1 (0.1)	1 (0.1)	0	0
Wound infection	0	0	1 (0.1)	1 (0.1)	0	0
Beta haemolytic streptococcal infection	0	0	0	0	1 (0.1)	0
Bronchitis	0	0	0	0	1 (0.1)	0
Cholecystitis infective	0	0	0	0	1 (0.1)	0
Encephalitis	0	0	0	0	0	1 (5.9)
Gastroenteritis	0	0	0	0	1 (0.1)	0
Pneumonia haemophilus	1 (0.4)	0	0	0	0	0
Postoperative abscess	0	0	0	0	1 (0.1)	0
Renal abscess	0	0	0	0	1 (0.1)	0
Respiratory syncytial virus bronchiolitis	0	0	0	0	1 (0.1)	0
Streptococcal sepsis	0	0	0	0	1 (0.1)	0
Injury, poisoning and procedural complications	**9 (3.7)**	**5 (0.9)**	**26 (1.9)**	**31 (1.6)**	**9 (0.6)**	**0**
Femur fracture	0	1 (0.2)	2 (0.1)	3 (0.2)	0	0
Ankle fracture	0	0	2 (0.1)	2 (0.1)	0	0
Lower limb fracture	0	0	2 (0.1)	2 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant	50 µg Matrix-M1	75 µg Matrix-M1	Any Dose Matrix-M1		
	N = 397	N = 853	N = 1489	N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Skin laceration	0	0	2 (0.1)	2 (0.1)	0	0
Accidental overdose	0	0	1 (0.1)	1 (0.1)	0	0
Coronary bypass stenosis	0	1 (0.2)	0	1 (0.1)	0	0
Face injury	0	0	1 (0.1)	1 (0.1)	0	0
Femoral neck fracture	0	0	1 (0.1)	1 (0.1)	0	0
Hip fracture	0	0	1 (0.1)	1 (0.1)	0	0
Injury	0	0	1 (0.1)	1 (0.1)	0	0
Multiple fractures	0	0	1 (0.1)	1 (0.1)	0	0
Periprosthetic fracture	0	0	1 (0.1)	1 (0.1)	0	0
Pneumothorax traumatic	0	0	1 (0.1)	1 (0.1)	0	0
Procedural pain	0	0	1 (0.1)	1 (0.1)	0	0
Pulmonary contusion	0	0	1 (0.1)	1 (0.1)	0	0
Rib fracture	0	0	1 (0.1)	1 (0.1)	0	0
Road traffic accident	0	0	1 (0.1)	1 (0.1)	0	0
Scapula fracture	0	0	1 (0.1)	1 (0.1)	0	0
Seroma	0	1 (0.2)	0	1 (0.1)	0	0
Soft tissue injury	0	1 (0.2)	0	1 (0.1)	0	0
Spinal column injury	0	0	1 (0.1)	1 (0.1)	0	0
Spinal fracture	1 (0.4)	0	1 (0.1)	1 (0.1)	2 (0.1)	0
Subdural haematoma	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Tibia fracture	0	0	1 (0.1)	1 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Traumatic haemothorax	0	0	1 (0.1)	1 (0.1)	0	0
Upper limb fracture	1 (0.4)	1 (0.2)	0	1 (0.1)	0	0
Cartilage injury	0	0	0	0	1 (0.1)	0
Contusion	1 (0.4)	0	0	0	0	0
Fall	0	0	0	0	1 (0.1)	0
Head injury	0	0	0	0	1 (0.1)	0
Incisional hernia	0	0	0	0	1 (0.1)	0
Laceration	3 (1.2)	0	0	0	0	0
Radius fracture	1 (0.4)	0	0	0	0	0
Sternal fracture	1 (0.4)	0	0	0	0	0
Tendon rupture	1 (0.4)	0	0	0	1 (0.1)	0
Wrist fracture	0	0	0	0	1 (0.1)	0
Nervous system disorders	**1 (0.4)**	**13 (2.4)**	**17 (1.3)**	**30 (1.6)**	**7 (0.5)**	**0**
Cerebrovascular accident	0	2 (0.4)	4 (0.3)	6 (0.3)	0	0
Embolic stroke	0	2 (0.4)	0	2 (0.1)	0	0
Ischaemic stroke	1 (0.4)	0	2 (0.1)	2 (0.1)	1 (0.1)	0
Seizure	0	2 (0.4)	0	2 (0.1)	0	0
Ataxia	0	0	1 (0.1)	1 (0.1)	0	0
Carotid artery disease	0	0	1 (0.1)	1 (0.1)	0	0
Cerebral arteriosclerosis	0	1 (0.2)	0	1 (0.1)	0	0
Cerebral infarction	0	0	1 (0.1)	1 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Cervical radiculopathy	0	1 (0.2)	0	1 (0.1)	0	0
Dementia alzheimer's type	0	1 (0.2)	0	1 (0.1)	0	0
Encephalopathy	0	0	1 (0.1)	1 (0.1)	0	0
Haemorrhage intracranial	0	0	1 (0.1)	1 (0.1)	0	0
Headache	0	1 (0.2)	0	1 (0.1)	0	0
Hemiparesis	0	0	1 (0.1)	1 (0.1)	0	0
Intracranial aneurysm	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Ischaemic cerebral infarction	0	1 (0.2)	0	1 (0.1)	0	0
Metabolic encephalopathy	0	0	1 (0.1)	1 (0.1)	0	0
Radiculopathy	0	1 (0.2)	0	1 (0.1)	0	0
Syncope	0	1 (0.2)	0	1 (0.1)	0	0
Transient aphasia	0	0	1 (0.1)	1 (0.1)	0	0
Transient global amnesia	0	0	1 (0.1)	1 (0.1)	0	0
Transient ischaemic attack	0	0	1 (0.1)	1 (0.1)	2 (0.1)	0
Carotid artery stenosis	0	0	0	0	1 (0.1)	0
Subarachnoid haemorrhage	0	0	0	0	2 (0.1)	0
Cardiac disorders	**2 (0.8)**	**10 (1.8)**	**10 (0.7)**	**20 (1.0)**	**19 (1.3)**	**0**
Cardiac failure congestive	0	2 (0.4)	4 (0.3)	6 (0.3)	4 (0.3)	0
Angina unstable	0	3 (0.5)	1 (0.1)	4 (0.2)	0	0
Atrial fibrillation	1 (0.4)	2 (0.4)	1 (0.1)	3 (0.2)	3 (0.2)	0
Coronary artery disease	1 (0.4)	0	3 (0.2)	3 (0.2)	2 (0.1)	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Acute myocardial infarction	0	2 (0.4)	0	2 (0.1)	2 (0.1)	0
Myocardial infarction	0	1 (0.2)	1 (0.1)	2 (0.1)	2 (0.1)	0
Acute coronary syndrome	0	0	0	0	1 (0.1)	0
Angina pectoris	0	0	0	0	3 (0.2)	0
Cardiac failure	0	0	0	0	1 (0.1)	0
Sinus node dysfunction	0	0	0	0	1 (0.1)	0
Gastrointestinal disorders	**3 (1.2)**	**11 (2.0)**	**8 (0.6)**	**19 (1.0)**	**18 (1.3)**	**0**
Hiatus hernia	0	1 (0.2)	2 (0.1)	3 (0.2)	0	0
Gastrointestinal haemorrhage	0	2 (0.4)	0	2 (0.1)	4 (0.3)	0
Abdominal pain upper	0	0	1 (0.1)	1 (0.1)	0	0
Colitis microscopic	0	1 (0.2)	0	1 (0.1)	0	0
Diverticulum	1 (0.4)	0	1 (0.1)	1 (0.1)	0	0
Duodenitis	0	1 (0.2)	0	1 (0.1)	1 (0.1)	0
Dysphagia	0	0	1 (0.1)	1 (0.1)	0	0
Enterovesical fistula	0	0	1 (0.1)	1 (0.1)	0	0
Gastric ulcer	0	0	1 (0.1)	1 (0.1)	0	0
Gastrooesophageal reflux disease	0	1 (0.2)	0	1 (0.1)	0	0
Gastroptosis	0	1 (0.2)	0	1 (0.1)	0	0
Intestinal perforation	1 (0.4)	1 (0.2)	0	1 (0.1)	0	0
Melaena	0	1 (0.2)	0	1 (0.1)	0	0
Oesophageal stenosis	0	1 (0.2)	0	1 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Pancreatitis	1 (0.4)	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Small intestinal obstruction	0	1 (0.2)	0	1 (0.1)	1 (0.1)	0
Abdominal pain	0	0	0	0	1 (0.1)	0
Colitis	0	0	0	0	2 (0.1)	0
Colonic fistula	0	0	0	0	1 (0.1)	0
Diverticulum intestinal haemorrhagic	0	0	0	0	1 (0.1)	0
Enterocutaneous fistula	0	0	0	0	1 (0.1)	0
Gastritis erosive	0	0	0	0	1 (0.1)	0
Gastrointestinal fistula	0	0	0	0	1 (0.1)	0
Haematochezia	0	0	0	0	1 (0.1)	0
Intestinal obstruction	0	0	0	0	1 (0.1)	0
Rectal prolapse	0	0	0	0	1 (0.1)	0
Respiratory, thoracic and mediastinal disorders	**0**	**4 (0.7)**	**13 (1.0)**	**17 (0.9)**	**11 (0.8)**	**0**
Respiratory failure	0	2 (0.4)	4 (0.3)	6 (0.3)	2 (0.1)	0
Acute respiratory failure	0	1 (0.2)	1 (0.1)	2 (0.1)	1 (0.1)	0
Chronic obstructive pulmonary disease	0	0	2 (0.1)	2 (0.1)	3 (0.2)	0
Pneumonia aspiration	0	0	2 (0.1)	2 (0.1)	0	0
Pulmonary embolism	0	1 (0.2)	1 (0.1)	2 (0.1)	3 (0.2)	0
Dyspnoea	0	0	1 (0.1)	1 (0.1)	0	0
Pleural effusion	0	0	1 (0.1)	1 (0.1)	0	0
Respiratory acidosis	0	0	1 (0.1)	1 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Acute respiratory distress syndrome	0	0	0	0	1 (0.1)	0
Hypoxia	0	0	0	0	1 (0.1)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**3 (1.2)**	**8 (1.5)**	**5 (0.4)**	**13 (0.7)**	**11 (0.8)**	**0**
Prostate cancer	0	1 (0.2)	1 (0.1)	2 (0.1)	0	0
Breast cancer	0	1 (0.2)	0	1 (0.1)	1 (0.1)	0
Endometrial cancer stage I	0	0	1 (0.1)	1 (0.1)	0	0
Gastric adenoma	0	1 (0.2)	0	1 (0.1)	0	0
Hormone receptor positive breast cancer	0	0	1 (0.1)	1 (0.1)	0	0
Invasive ductal breast carcinoma	0	1 (0.2)	0	1 (0.1)	0	0
Lung cancer metastatic	0	1 (0.2)	0	1 (0.1)	0	0
Malignant melanoma	0	0	1 (0.1)	1 (0.1)	0	0
Metastatic neoplasm	0	0	1 (0.1)	1 (0.1)	0	0
Metastatic squamous cell carcinoma	0	1 (0.2)	0	1 (0.1)	0	0
Non-small cell lung cancer metastatic	0	1 (0.2)	0	1 (0.1)	0	0
Renal cancer stage I	0	1 (0.2)	0	1 (0.1)	0	0
Adenocarcinoma of colon	0	0	0	0	1 (0.1)	0
Benign ovarian tumour	0	0	0	0	1 (0.1)	0
Bladder transitional cell carcinoma	0	0	0	0	1 (0.1)	0
Follicular thyroid cancer	0	0	0	0	1 (0.1)	0
Leiomyosarcoma	0	0	0	0	1 (0.1)	0
Lung carcinoma cell type unspecified stage IV	0	0	0	0	1 (0.1)	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant	50 µg Matrix-M1	75 µg Matrix-M1	Any Dose Matrix-M1		
	N = 397	N = 853	N = 1489	N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Lung neoplasm malignant	0	0	0	0	1 (0.1)	0
Malignant peritoneal neoplasm	1 (0.4)	0	0	0	0	0
Meningioma	1 (0.4)	0	0	0	0	0
Renal cell carcinoma recurrent	0	0	0	0	1 (0.1)	0
Small cell lung cancer	0	0	0	0	1 (0.1)	0
Squamous cell carcinoma of the tongue	1 (0.4)	0	0	0	0	0
Transitional cell carcinoma	0	0	0	0	1 (0.1)	0
Musculoskeletal and connective tissue disorders	**2 (0.8)**	**3 (0.5)**	**7 (0.5)**	**10 (0.5)**	**9 (0.6)**	**0**
Osteoarthritis	1 (0.4)	1 (0.2)	2 (0.1)	3 (0.2)	5 (0.4)	0
Back pain	0	0	2 (0.1)	2 (0.1)	0	0
Intervertebral disc protrusion	0	1 (0.2)	1 (0.1)	2 (0.1)	1 (0.1)	0
Arthralgia	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Rhabdomyolysis	0	0	1 (0.1)	1 (0.1)	0	0
Spinal pain	0	1 (0.2)	0	1 (0.1)	0	0
Arthritis	0	0	0	0	1 (0.1)	0
Pain in extremity	0	0	0	0	1 (0.1)	0
Vertebral osteophyte	1 (0.4)	0	0	0	0	0
General disorders and administration site conditions	**1 (0.4)**	**4 (0.7)**	**5 (0.4)**	**9 (0.5)**	**1 (0.1)**	**0**
Death	0	1 (0.2)	2 (0.1)	3 (0.2)	0	0
Chest pain	0	2 (0.4)	0	2 (0.1)	0	0
Asthenia	0	0	1 (0.1)	1 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Chest discomfort	0	1 (0.2)	0	1 (0.1)	0	0
Complication associated with device	0	0	1 (0.1)	1 (0.1)	0	0
Non-cardiac chest pain	0	0	1 (0.1)	1 (0.1)	0	0
Hernia	1 (0.4)	0	0	0	0	0
Pyrexia	0	0	0	0	1 (0.1)	0
Vascular disorders	**0**	**1 (0.2)**	**8 (0.6)**	**9 (0.5)**	**4 (0.3)**	**1 (5.9)**
Deep vein thrombosis	0	0	2 (0.1)	2 (0.1)	1 (0.1)	0
Accelerated hypertension	0	0	1 (0.1)	1 (0.1)	0	0
Aortic aneurysm	0	0	1 (0.1)	1 (0.1)	0	0
Aortic aneurysm rupture	0	1 (0.2)	0	1 (0.1)	0	0
Aortic stenosis	0	0	1 (0.1)	1 (0.1)	0	0
Hypertension	0	0	1 (0.1)	1 (0.1)	0	0
Hypertensive urgency	0	0	1 (0.1)	1 (0.1)	0	0
Thrombosis	0	0	1 (0.1)	1 (0.1)	0	0
Aortic dissection	0	0	0	0	0	1 (5.9)
Arterial spasm	0	0	0	0	1 (0.1)	0
Hypotension	0	0	0	0	1 (0.1)	0
Shock haemorrhagic	0	0	0	0	1 (0.1)	0
Metabolism and nutrition disorders	**1 (0.4)**	**5 (0.9)**	**3 (0.2)**	**8 (0.4)**	**4 (0.3)**	**0**
Dehydration	0	2 (0.4)	1 (0.1)	3 (0.2)	1 (0.1)	0
Electrolyte imbalance	0	0	2 (0.1)	2 (0.1)	0	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Diabetic ketoacidosis	0	1 (0.2)	0	1 (0.1)	0	0
Failure to thrive	0	1 (0.2)	0	1 (0.1)	0	0
Hypokalaemia	0	1 (0.2)	0	1 (0.1)	0	0
Fluid overload	0	0	0	0	1 (0.1)	0
Hyponatraemia	0	0	0	0	1 (0.1)	0
Type 2 diabetes mellitus	1 (0.4)	0	0	0	1 (0.1)	0
Hepatobiliary disorders	0	4 (0.7)	2 (0.1)	6 (0.3)	2 (0.1)	0
Cholelithiasis	0	2 (0.4)	0	2 (0.1)	0	0
Cholecystitis	0	1 (0.2)	0	1 (0.1)	0	0
Hepatic cirrhosis	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Hepatic cyst	0	1 (0.2)	0	1 (0.1)	0	0
Ischaemic hepatitis	0	0	1 (0.1)	1 (0.1)	0	0
Bile duct stone	0	0	0	0	1 (0.1)	0
Renal and urinary disorders	**0**	**0**	**4 (0.3)**	**4 (0.2)**	**5 (0.4)**	**0**
Acute kidney injury	0	0	3 (0.2)	3 (0.2)	2 (0.1)	0
Calculus urinary	0	0	1 (0.1)	1 (0.1)	0	0
Anuria	0	0	0	0	1 (0.1)	0
Renal failure	0	0	0	0	1 (0.1)	0
Ureterolithiasis	0	0	0	0	1 (0.1)	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator N = 1551	Placebo N = 18
	Without Matrix-M1 Adjuvant N = 397	50 µg Matrix-M1 N = 853	75 µg Matrix-M1 N = 1489	Any Dose Matrix-M1 N = 2342		
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Blood and lymphatic system disorders	**1 (0.4)**	**2 (0.4)**	**1 (0.1)**	**3 (0.2)**	**4 (0.3)**	**0**
Anaemia	0	2 (0.4)	0	2 (0.1)	2 (0.1)	0
Blood loss anaemia	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0
Iron deficiency anaemia	1 (0.4)	0	0	0	0	0
Leukocytosis	0	0	0	0	1 (0.1)	0
Product issues	**0**	**1 (0.2)**	**0**	**1 (0.1)**	**0**	**0**
Device dislocation	0	1 (0.2)	0	1 (0.1)	0	0
Psychiatric disorders	**0**	**0**	**1 (0.1)**	**1 (0.1)**	**1 (0.1)**	**0**
Hallucination, visual	0	0	1 (0.1)	1 (0.1)	0	0
Mental status changes	0	0	0	0	1 (0.1)	0
Reproductive system and breast disorders	**0**	**1 (0.2)**	**0**	**1 (0.1)**	**1 (0.1)**	**0**
Benign prostatic hyperplasia	0	1 (0.2)	0	1 (0.1)	0	0
Prostatomegaly	0	0	0	0	1 (0.1)	0
Skin and subcutaneous tissue disorders	**0**	**1 (0.2)**	**0**	**1 (0.1)**	**0**	**0**
Angioedema	0	1 (0.2)	0	1 (0.1)	0	0
Endocrine disorders	**0**	**0**	**0**	**0**	**1 (0.1)**	**0**
Goitre	0	0	0	0	1 (0.1)	0

Table 32: Summary of Exposure-Adjusted Event Rates (Per 100 Subject-Years) of Serious Adverse Events in Participants ≥ 65 Years of Age

MedDRA Version 23.0 System Organ Class/Preferred Term	Vaccine Antigen				Active Influenza Vaccine Comparator	Placebo
	Without Matrix-M1 Adjuvant	50 µg Matrix-M1	75 µg Matrix-M1	Any Dose Matrix-M1		
	N = 397	N = 853	N = 1489	N = 2342	N = 1551	N = 18
Total exposure (SY)	**240.97**	**551.00**	**1357.34**	**1908.34**	**1419.84**	**16.91**
Mean exposure (days)	**221.7**	**235.9**	**332.9**	**297.6**	**334.4**	**343.2**
Median exposure (days)	**183**	**183**	**351**	**350**	**351**	**386**
Eye disorders	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**
Macular fibrosis	0	0	0	0	0	1 (5.9)
Immune system disorders	**0**	**0**	**0**	**0**	**1 (0.1)**	**0**
Hypersensitivity	0	0	0	0	1 (0.1)	0

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment-emergent adverse event; SY = subject-years.

Note: Overall exposure was summarized in total SY. This was calculated as follows: SY = sum of duration of exposure in days (for all participants in each vaccine group)/365.25. Unsolicited adverse events were summarized by frequencies and exposure-adjusted event rates (ERs). ERs per 100 SY were calculated by dividing the total number of participants experiencing the unsolicited adverse event by the sum of all participants' time (in 100 years) of exposure during the vaccine follow-up period. The entire exposure time during the vaccine follow-up period was used.

5.4 Other Significant Adverse Events

PIMMCs were considered AESIs across the Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant. Since all reported PIMMCs were reported as SAEs, analysis of PIMMCs are presented in Section 5.3.

5.5 Analysis of Adverse Events by Organ System of Syndrome

A total of 445 SAEs were reported in 4,725 participants, with 35 events reported in 417 participants 18 to 64 years of age (see Section 5.3.1 for details) and 410 events reported in 4,308 participants ≥ 65 years of age (see Section 5.3.2 for details). In participants 18 to 64 years of age, the highest number of SAEs was reported in the SOCs of Infections and Infestations and Neoplasms Benign, Malignant and Unspecified (including cysts and polyps), with all events occurring once for each preferred term. In participants ≥ 65 years of age, the highest number of SAEs was reported in the SOC of Infections and Infestations, with similar exposure-adjusted rates across the Any Dose Matrix-M1-adjuvanted vaccine (3.0 events per 100 SY), Without Matrix-M1-adjuvanted vaccine (2.1 events per 100 SY), and Active Influenza Vaccine Comparator (2.2 events per 100 SY) groups but all lower than in the Placebo group (5.9 events per 100 SY). No pattern emerged across the SAEs for any of the treatment groups.

There were 2 SAEs (pericarditis and convulsion) assessed by the investigator as related to study treatment, with both events reported in the Without Matrix-M1-adjuvanted vaccine group (see Section 5.3.1 for details).

There were 4 SAEs (all seizure) reported as PIMMCs, with 2 events each occurring in each age strata. In participants 18 to 64 years of age, both seizure events (2.1 events per 100 SY) were reported in the Without Matrix-M1-adjuvanted vaccine group; in participants ≥ 65 years of age, both seizure events were reported in the 50 µg Matrix-M1-adjuvanted vaccine group.

6 DISCUSSION AND CONCLUSIONS

SARS-CoV-2 rS with Matrix-M1 adjuvant is being evaluated in 5 ongoing clinical trials. Safety data from each of these trials will be provided in individual interim reports but will not be pooled in an integrated summary of safety due to the urgent need to rapidly prepare data for regulatory submissions during the ongoing global coronavirus pandemic. To supplement the lack of available long-term safety data (≥ 6 months) in the ongoing clinical trials of SARS-CoV-2 rS with Matrix-M1 adjuvant, an integrated analysis of safety was performed in 2,574 adult participants 18 years of age and older across 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens using the same manufacturing platform technology as SARS-CoV-2 rS administered with the same Matrix-M1 adjuvant with safety follow-up ranging from 6 months to 1 year. For this integrated analysis, short-term safety data (ie, solicited local and systemic TEAEs and unsolicited TEAEs) were summarized for each individual study and long-term safety data (ie, SAEs and AESIs) were pooled across the clinical trials.

Safety summaries of the 5 individual Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant showed that each antigen and adjuvant regimen was acceptably well tolerated and resulted in safety profiles similar to those seen in the clinical trials of SARS-CoV-2 rS with Matrix-M1 adjuvant. In general, frequencies of solicited local and systemic TEAEs were increased in recipients who received Matrix-M1-adjuvanted vaccines (compared to those who received vaccines without Matrix-M1 adjuvant) and in recipients who received two-dose regimens of Matrix-M1-adjuvanted vaccine (compared to those who received one-dose regimens of Matrix-M1-adjuvanted vaccine). Severe solicited TEAEs were reported in less than 10% of participants across the two-dose Matrix-M1-adjuvanted vaccine groups and in less than 5% of participants across the one-dose Matrix-M1-adjuvanted vaccine groups. Frequencies of unsolicited TEAEs were generally similar between the treatment groups and occurred in less than 10% of participants in Studies EBOV-H-101, tNIV-E-101, qNIV-E-201, and qNIV-E-301 and less than 30% of participants in Study RSV-E-205.

Safety analyses of pooled SAE and AESI data across the 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant showed no increased risks between the treatment groups across the two age strata evaluated (ie, 18 to 64 years and ≥ 65 years). Approximately 0.5% of participants in the Matrix-M1-adjuvanted vaccine and active influenza comparator groups died, which was lower than the percentage of death (1.4%) in the placebo group. All deaths occurred in participants ≥ 65 years, with diagnoses that were generally expected for this age population and consistent with participants' medical histories; none of the deaths was assessed as related to treatment. In participants 18 to 64 years of age, frequencies of other SAEs occurred at similar exposure-adjusted rates across the Matrix-M1-adjuvanted vaccine (9.3 events per 100 SY), Matrix-M1-unadjuvanted vaccine (10.4 events per 100 SY), and active influenza vaccine comparator (13.1 events per 100 SY) groups, all of which had higher exposure-adjusted rates than placebo (0 events per 100 SY). Two SAEs (pericarditis and convulsion) were assessed by the investigator as related to study treatment, both of which occurred in the Without Matrix-M1-adjuvanted vaccine group; however, upon careful review of the participants' medical histories, the sponsor deemed the events as not related to trial vaccine. In participants ≥ 65 years of age, frequencies of other SAEs also occurred at similar exposure-adjusted rates across the Any Dose Matrix-M1-adjuvanted vaccine (12.6 events per 100 SY), Without Matrix-M1-adjuvanted vaccine (11.6 events per 100 SY), and Active Influenza Vaccine

Comparator (9.8 events per 100 SY) groups, all of which had lower exposure-adjusted rates than Placebo (17.7 events per 100 SY). There were 4 SAEs (all seizure) reported as PIMMCs, with 2 events each occurring in each age strata. In participants 18 to 64 years of age, both seizure events (2.1 events per 100 SY) were reported in the Without Matrix-M1-adjuvanted vaccine group; in participants ≥ 65 years of age, both seizure events were reported in the 50 µg Matrix-M1-adjuvanted vaccine group.

In conclusion, both short- and long-term safety data from other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant were acceptably well tolerated in healthy and medically stable participants 18 years of age and older. In the short-term, these safety profiles appear similar to those seen across clinical trials with SARS-CoV-2 rS with Matrix-M1 adjuvant. In the long-term, no increased risk was associated with any of the recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant supporting a favorable long-term safety profile of SARS-CoV-2 rS with Matrix-M1 adjuvant.

7 NARRATIVES

A listing of SAEs across the 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant is presented in Appendix 1. Narratives of deaths, treatment-related SAEs, and serious PIMMCs are presented in Appendix 2.

8 REFERENCES

None.

9 APPENDIX

Appendix 1 Listing of Serious Adverse Events

Appendix 2 Narratives of Deaths, Treatment-Related Serious Adverse Events, and Important Adverse Events of Special Interest

APPENDIX 1 LISTING OF SERIOUS ADVERSE EVENTS

NOVAVAX
Creating Tomorrow's Vaccines Today

Serious Adverse Event (SAE) Line Listing

01-JAN-2014 To 17-MAR-2021

EBOV-H-101, RSV-E-205, tNIV-E-101, qNIV-E-201, qNIV-E-301

Protocol # EBOV-H-101

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	EBOV GP 13µg and 50µg Matrix-M1 (11Feb15); EBOV GP 0µg and 0µg Matrix-M1 (06Mar15)	UK0270144	18-29 Year(s) Male		Collapse (Loss of consciousness)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17-Aug-15	24-Aug-15	Recovered/Resolved with sequelae	Not Related	Not Related
TKE-802742060	EBOV GP 6.5µg and 50µg Matrix-M1 (11Feb15); EBOV GP 0µg and 0µg Matrix-M1 (05Mar15)	US050-1072	18-29 Year(s) Female		Thrombosed haemorrhoid (Haemorrhoids thrombosed)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jul-15	19 Aug 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	EBOV GP 13µg and 0µg Matrix-M1 (11Feb15; 04Mar15)	US050-1073	30-39 Year(s) Male		Seizure (Convulsion)	Nervous system disorders	Severe	Medically significant event	12-Aug-15	13-Aug-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	EBOV GP 25µg and 50µg Matrix-M1 (11Feb15); EBOV GP 0µg and 0µg Matrix-M1 (04Mar15)	US050-1091	40-49 Year(s) Female		Cellulitis (Cellulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	29 Jun 2015	14-Jul-15	Recovered/Resolved with sequelae	Not Related	Not Related
IHG-548185183	EBOV GP 6.5µg and 0µg Matrix-M1 (11Feb15; 04Mar15)	US045-1151	30-39 Year(s) Male		Pericarditis (Pericarditis)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	04 Sep 2015	25-Dec-15	Recovered/Resolved	B - Possible/Medium	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	EBOV GP 50µg and 50µg Matrix-M1 (11Feb15); EBOV GP 0µg and 0µg Matrix-M1 (04Mar15)	US050-1050	18-29 Year(s) Male		Superficial face and hand abrasions (Skin abrasion)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04-Mar-15	16 Aug 2015	Recovered/Resolved	Not Related	Not Related
					PPD injuries with multiple front fractured PPD (PPD injury)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04-Mar-15	16 Aug 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	EBOV GP 13µg and 50µg Matrix-M1 (11Feb15; 05Mar15)	US050-1061	40-49 Year(s) Female		Gall bladder polyps (Gallbladder polyp)	Hepatobiliary disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07-Feb-16	07-Feb-16	Recovered/Resolved	Not Related	Not Related
HRV-151283347	EBOV GP 13µg and 0µg Matrix-M1 (11Feb15; 04Mar15)	US050-1073	30-39 Year(s) Male		Seizure (Convulsion)	Nervous system disorders	Moderate	Medically significant event	22-Dec-15	22-Dec-15	Recovered/Resolved	B - Possible/Medium	Not Related

Protocol # qNIV-E-201

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 11Mar15)	US004-1048	80-89 Year(s) Male		Melanoma (Malignant melanoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Medically significant event	27-Feb-15	05-Mar-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	US030-1028	70-79 Year(s) Male		Right middle cerebral artery distribution subcortical stroke (Cerebrovascular accident)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	18-Feb-15	18-Feb-15	Recovered/Resolved with sequelae	Not Related	Not Related
VOY-787546461	Fluzone HD (11Feb15)	US012-1092	90 or older Year(s) Female		Dehydration (Dehydration)	Metabolism and nutrition disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07 Mar 2015	11-Mar-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087448	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	AU006-3029	70-79 Year(s) Female		Duodenitis (Duodenitis)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07-Mar-15	09-Mar-15	Recovered/Resolved	Not Related	Not Related
					GI bleed (Gastrointestinal haemorrhage)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07-Mar-15	09-Mar-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15)	AU006-2009	70-79 Year(s) Male		Diverticulitis of colon (Diverticulitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	27 Feb 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Flublok Quadrivalent (11Feb15; 11Mar15)	US108-1054	60-69 Year(s) Male	19-Mar-15	Death related to PPD (Road traffic accident)	Injury, poisoning and procedural complications	Severe	Death	19-Mar-15	19-Mar-15	Death	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 09Mar15)	US017-1069	70-79 Year(s) Female		Gastroptosis (Gastroptosis)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	14-Feb-15	15-Mar-15	Recovered/Resolved	Not Related	Not Related
					Paraesophageal hernia (Hiatus hernia)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	14-Feb-15	15-Mar-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 10Mar15)	US029-1064	70-79 Year(s) Male		Community Acquired Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	21-Mar-15	06-Apr-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 13Mar15)	US029-1104	80-89 Year(s) Female		Urinary tract infection (Urinary tract infection)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	04 Mar 2015	07 Mar 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 300 µg + Matrix-M1 50 µg (26Jun15; 22Jul15)	US029-1139	70-79 Year(s) Male	23-Nov-15	Dehydration (Dehydration)	Metabolism and nutrition disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03-Nov-15	07 Nov 2015	Recovered/Resolved	Not Related	Not Related
					Failure to thrive (Failure to thrive)	Metabolism and nutrition disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03-Nov-15	07 Nov 2015	Recovered/Resolved	Not Related	Not Related
					Hypokalemia (Hypokalaemia)	Metabolism and nutrition disorders		In-patient hospitalisation;In-Patient Hospitalisation	03-Nov-15	07 Nov 2015	Recovered/Resolved	Not Related	Not Related
					Right lung cancer, metastatic to bone and brain (Lung cancer metastatic)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Death	30-Jun-15	23-Nov-15	Death	Not Related	Not Related
					Syncopal episode (Syncope)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Oct-15	26-Oct-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 09Mar15)	US017-1069	70-79 Year(s) Female		Perforated bowel (Intestinal perforation)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	27 Mar 2015	27 Mar 2015	Recovered/Resolved	Not Related	Not Related
					Post-operative esophageal strictures (Oesophageal stenosis)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	01 Apr 2015	01 Apr 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 09Mar15)	US013-1154	60-69 Year(s) Female		Malignant neoplasm in right breast (Breast cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	Life threatening	09-Mar-15		Not Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone HD (11Feb15; 09Mar15)	US030-1156	70-79 Year(s) Female		Pneumonia of left lower lobe due to infectious organism (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03 Apr 2015	23-Apr-15	Recovered/Resolved	Not Related	Not Related
					Streptococcal septicemia (Streptococcal sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03 Apr 2015	07-Apr-15	Recovered/Resolved	Not Related	Not Related
					COPD with acute exacerbation (Chronic obstructive pulmonary disease)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03 Apr 2015	23-Apr-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Flublok Quadrivalent (11Feb15; 11Mar15)	US018-1116	80-89 Year(s) Female		PPD fracture (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Mar-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Fracture of PPD (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Mar-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Ligamentous injury (Ligament injury)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Mar-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 11Mar15)	US018-1087	70-79 Year(s) Female		Embolic stroke involving left middle cerebral artery (Embolic stroke)	Vascular disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Mar-15	28-Mar-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg (11Feb15; 11Mar15)	US017-1032	70-79 Year(s) Female		Broken PPD (PPD fracture)	Injury, poisoning and procedural complications	Severe	Disabled;In-patient hospitalisation;In-Patient Hospitalisation	20-Mar-15	27-Mar-15	Recovered/Resolved	Not Related	Not Related
JVO-036087748	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15)	AU004-1029	70-79 Year(s) Female		Worsening of right knee osteoarthritis (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	12-Mar-15		Not Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 11Mar15)	US066-1131	70-79 Year(s) Female		Urolithiasis with obstruction (Calculus urinary)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	31 Mar 2015	01 Apr 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	US066-1134	70-79 Year(s) Female		Worsening of anemia (Anaemia)	Blood and lymphatic system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 Mar 2015	30 Mar 2015	Recovered/Resolved	Not Related	Not Related
					GI bleed (Gastrointestinal haemorrhage)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 Mar 2015	30 Mar 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone HD (11Feb15; 09Mar15)	US017-1073	70-79 Year(s) Female		Chest pain- Cardiac (Angina pectoris)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07-Apr-15	08-Apr-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 12Mar15)	US004-1054	70-79 Year(s) Female		Cellulitis bilateral lower legs (Cellulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	24 Apr 2015	02-May-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 13Mar15)	US108-1046	60-69 Year(s) Female		Appendicitis (Appendicitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	22 Apr 2015	26 Apr 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone HD (11Feb15; 10Mar15)	US013-1104	60-69 Year(s) Female		Bronchitis (Bronchitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	20-Apr-15	22-Apr-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 13Mar15)	US017-1031	60-69 Year(s) Male		Bilateral trauma pneumothoraces LSR (Pneumothorax traumatic)	Injury, poisoning and procedural complications	Moderate	Disabled;In-patient hospitalisation;In-Patient Hospitalisation	16-Apr-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Fractured scapula (Scapula fracture)	Injury, poisoning and procedural complications	Moderate	Disabled;In-patient hospitalisation;In-Patient Hospitalisation	16-Apr-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
					T6 superior endplate deformity (Spinal column injury)	Injury, poisoning and procedural complications	Moderate	Disabled;In-patient hospitalisation;In-Patient Hospitalisation	16-Apr-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Fractured L2 transverse process (Spinal fracture)	Injury, poisoning and procedural complications	Moderate	Disabled;In-patient hospitalisation;In-Patient Hospitalisation	16-Apr-15	03 Jun 2015	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 12Mar15)	AU004-1024	70-79 Year(s) Male		Unstable angina pectoris (Angina unstable)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	14-Apr-15	21-Apr-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 12Mar15)	AU006-1085	80-89 Year(s) Female		Myocardial infarction (Myocardial infarction)	Cardiac disorders	Mild	In-patient hospitalisation;In-Patient Hospitalisation	28-Apr-15	28-Apr-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 13Mar15)	AU006-1060	70-79 Year(s) Female		Diabetic ketoacidosis (Diabetic ketoacidosis)	Metabolism and nutrition disorders	Mild	In-patient hospitalisation;In-Patient Hospitalisation	10-May-15	26 May 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 11Mar15)	US018-1087	70-79 Year(s) Female		Embolic stroke involving left middle cerebral artery (Embolic stroke)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Apr-15	29-Apr-15	Recovered/Resolved with sequelae	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 11Mar15)	US025-1134	60-69 Year(s) Female		MSSA/staph lugdenesis infection (Staphylococcal infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Acute chronic obstructive pulmonary disease exacerbation (Chronic obstructive pulmonary disease)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Apr-15	18-Apr-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg (11Feb15; 11Mar15)	US004-1016	60-69 Year(s) Female		Onset of Corohary artery disease (Coronary artery disease)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	15-Apr-15		Not Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 13Mar15)	US106-1080	60-69 Year(s) Female	26-Apr-15	Death-Unknown etiology (Death)	General disorders and administration site conditions	Severe	Death	26-Apr-15	26-Apr-15	Death	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 11Mar15)	US079-1058	60-69 Year(s) Female		Intracranial aneurysm (Intracranial aneurysm)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	15-Apr-15	29-Apr-15	Recovered/Resolved with sequelae	Not Related	Not Related
WEI-274448216	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 12Mar15)	US012-1013	70-79 Year(s) Female		Influenza A (Influenza)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Jun-15	13-Jun-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 11Mar15)	US029-1006	60-60-69 Year(s) Female	20-Jun-15	Thoracoabdominal aneurysm (Aortic aneurysm rupture)	Vascular disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation	20-Jun-15	20-Jun-15	Death	Not Related	Not Related
TKE-802742060	Fluzone HD (11Feb15; 10Mar15)	US029-1023	80-89 Year(s) Female		Worsening of Type 2 Diabetes (Type 2 diabetes mellitus)	Metabolism and nutrition disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Jun-15	27 Jun 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 11Mar15)	US004-1088	60-69 Year(s) Male		Worsening Benign prostatic hyperplasia (Benign prostatic hyperplasia)	Reproductive system and breast disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	03 Jun 2015	03 Jul 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	US004-1009	80-89 Year(s) Male	13-May-15	Small bowel obstruction (Small intestinal obstruction)	Gastrointestinal disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation	07 May 2015	13-May-15		Not Related	Not Related
					Pulmonary embolism (Pulmonary embolism)	Respiratory, thoracic and mediastinal disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-May-15	13-May-15	Death	Not Related	Not Related
					Hypoxic hypercapnic respiratory failure (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-May-15	13-May-15	Death	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 10Mar15)	US018-1081	70-79 Year(s) Male		Chest discomfort (Non-cardiac) (Chest discomfort)	General disorders and administration site conditions	Severe	In-patient hospitalisation;In-Patient Hospitalisation	05-Jul-15	06-Jul-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg (11Feb15; 10Mar15)	US004-1003	60-69 Year(s) Male		Squamous cell carcinoma-oral cancer (location:base of PPD) (Squamous cell carcinoma of the PPD)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Medically significant event	13 Jul 2015		Not Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 10Mar15)	US029-1017	70-79 Year(s) Female		Worsening of seizure disorder (Seizure)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jul-15	25-Jul-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 11Mar15)	US025-1006	70-79 Year(s) Female		Influenzal bronchitis (Bronchitis viral)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27-Jul-15	08-Aug-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27-Jul-15	08-Aug-15	Recovered/Resolved	Not Related	Not Related
					Sepsis (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27-Jul-15	08-Aug-15	Recovered/Resolved	Not Related	Not Related
GCL-653380502	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 09Mar15)	US004-1079	80-80-89 Year(s) Male		Diverticulitis (Diverticulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	13 Jul 2015	16 Jul 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg (11Feb15; 10Mar15)	US106-1024	70-79 Year(s) Female		Worsening of right knee osteoarthritis (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	30-Jun-15	02-Jul-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	US025-1161	70-79 Year(s) Male		Seizure (Seizure)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	24-Jul-15	25-Jul-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone HD (11Feb15; 11Mar15)	US012-1064	80-80-89 Year(s) Male		Lacerated PPD injury (PPD injury)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Aug 2015	26-Aug-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 12Mar15)	US004-1100	60-69 Year(s) Female		Gallstones (Cholelithiasis)	Hepatobiliary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	07-Jul-15	11-Jul-15	Recovered/Resolved	Not Related	Not Related
					Hepatic cyst on liver (Hepatic cyst)	Hepatobiliary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	07-Jul-15	11-Jul-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 10Mar15)	US025-1127	80-89 Year(s) Female	09-Jul-15	Cerebral atherosclerosis (Cerebral arteriosclerosis)	Nervous system disorders	Severe	Death	05 Jun 2015	09-Jul-15	Death	Not Related	Not Related
					Late onset of Alzheimer's disease (Dementia Alzheimer's type)	Nervous system disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation	16-Jun-15	09-Jul-15	Death	Not Related	Not Related
					Acute ischemic left MCA stroke (Ischaemic cerebral infarction)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	05 Jun 2015	05 Jun 2015	Recovered/Resolved	Not Related	Not Related
JYO-038087748	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 12Mar15)	AU006-2015	70-79 Year(s) Male	02 Jun 2015	Acute non ST segment elevation myocardial infarction (Acute myocardial infarction)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-May-15	18-May-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Hypoxemic respiratory failure (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	Death	02 Jun 2015	02 Jun 2015	Death	Not Related	Not Related
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 13Mar15)	US004-1091	60-69 Year(s) Female		Clostridium difficile infection (Clostridium difficile infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	17-Apr-15	30 Apr 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg (11Feb15; 11Mar15)	US029-1144	70-79 Year(s) Male		Cellulitis of PPD (Cellulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Jul-15	23-Aug-15	Recovered/Resolved	Not Related	Not Related
					Sepsis due to unspecified organism (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Jul-15	23-Aug-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 09Mar15)	AU006-1077	70-79 Year(s) Female		Broken PPD (PPD fracture)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	08 Jul 2015	10 Jul 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 10Mar15)	US029-1090	60-69 Year(s) Female		Dehydration (Dehydration)	Metabolism and nutrition disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	06-Aug-15	10-Aug-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 11Mar15)	US025-1134	60-69 Year(s) Female		Epigastric pain (Abdominal pain upper)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07-Jun-15	07-Jun-15	Recovered/Resolved	Not Related	Not Related
					Dysphagia (Dysphagia)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07-Jun-15	07-Jun-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 10Mar15)	US025-1127	80-89 Year(s) Female		Atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27-May-15	09-Jul-15	Recovered/Resolved	Not Related	Not Related
					Acute cardiac chest pain (Chest pain)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-May-15	28-May-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg (11Feb15; 11Mar15)	US030-1078	70-79 Year(s) Female		Pancreatitis (Pancreatitis)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Jun 2015	05 Jun 2015	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 10Mar15)	US029-1097	70-79 Year(s) Male		Worsening of gastroesophageal reflux disease (Gastrooesophageal reflux disease)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Aug-15	09-Aug-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 13Mar15)	US025-1058	70-79 Year(s) Male		Pain assoicated with pathologic fracture of thoracic vertebrate (T5) (Spinal pain)	General disorders and administration site conditions	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	27 Jul 2015		Not Recovered/Resolved	Not Related	Not Related
					Metastatic non-small cell lung cancer (Non-small cell lung cancer metastatic)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Life threatening	07-Jul-15		Not Recovered/Resolved	Not Related	Not Related
HRV-151283347	Flublok Quadrivalent (11Feb15; 10Mar15)	US029-1127	70-79 Year(s) Male		Community acquired pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jul-15	31 Jul 2015	Recovered/Resolved	Not Related	Not Related
					Sepsis (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jul-15	21-Jul-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15; 27Feb15)	US079-1084	70-79 Year(s) Female		Cerebrovascular accident (Cerebrovascular accident)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	30 Apr 2015	* 30-May-15	* Recovered/Resolved with sequelae	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 50 µg (co-form) (11Feb15; 11Mar15)	US030-1012	60-69 Year(s) Male		Losartan induced angioedema (Angioedema)	Immune system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jul-15	25-Jul-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	US004-1012	70-79 Year(s) Female		Exacerbation of congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	28 Jul 2015	04 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Acute hypoxic respiratory failure (Acute respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	28 Jul 2015	04 Aug 2015	Recovered/Resolved	Not Related	Not Related
JYO-036087748	Quad-NIV 300 µg + Matrix-M1 50 µg (11Feb15; 11Mar15)	US004-1045	70-79 Year(s) Male		Diverticulitis (Diverticulitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	26 Jun 2015	28 Jun 2015	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 50 µg (in-clinic) (11Feb15; 14Mar15)	US004-1005	80-89 Year(s) Female		Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	02 Jun 2015	05 Jun 2015	Recovered/Resolved	Not Related	Not Related

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Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US003-1030	70-79 Year(s) Male	15-Feb-15	Cardiac stent collapse (Complication associated with device)	General disorders and administration site conditions	Severe	Death	15-Feb-15	15-Feb-15	Death	Not Related	Not Related
					Decompensated cirrhotic liver disease (Hepatic cirrhosis)	Hepatobiliary disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	11-Feb-15	15-Feb-15		Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1064	60-60-69 Year(s) Female		Left sided weakness (Hemiparesis)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Mar 2015	06 Mar 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US017-1142	60-69 Year(s) Male		Worsening of coronary artery disease (Coronary artery disease)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	03 Mar 2015	10-Mar-15	Recovered/Resolved	Not Related	Not Related
					Worsening of aortic stenosis (Aortic stenosis)	Vascular disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	02 Mar 2015	10-Mar-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US056-1071	60-69 Year(s) Female		PPD broken PP (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Mar 2015	08-Mar-15	Recovered/Resolved with sequelae	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US078-1045	80-89 Year(s) Male		Acute infection PPD (Localised infection)	Infections and infestations	Moderate	Medically significant event	02 Mar 2015	16-Jun-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US138-1051	80-89 Year(s) Male		Adenocarcinoma of prostate (Prostate cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	Medically significant event	19-Feb-15		Not Recovered/Resolved	Not Related	Not Related
WEI-274448216	Fluzone Quadrivalent (11Feb15)	US012-1136	70-79 Year(s) Male										

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Acute anemia blood loss (Blood loss anaemia)	Blood and lymphatic system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	23-Feb-15	25-Feb-15	Recovered/Resolved	Not Related	Not Related
					Diverticular bleed (Diverticulum intestinal haemorrhagic)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	16-Feb-15	18-Feb-15	Recovered/Resolved	Not Related	Not Related
					Gastrointestinal bleed (Gastrointestinal haemorrhage)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	16-Feb-15	18-Feb-15	Recovered/Resolved	Not Related	Not Related
					Hematochezia (Haematochezia)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	16-Feb-15	18-Feb-15	Recovered/Resolved	Not Related	Not Related
					Hypotension (Hypotension)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	16-Feb-15	18-Feb-15	Recovered/Resolved with sequelae	Not Related	Not Related
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US013-1005	70-79 Year(s) Female		PPD infection (Localised infection)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	17-Feb-15	09-Mar-15	Recovered/Resolved	Not Related	Not Related
					Pulmonary contusion (Pulmonary contusion)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	17-Feb-15	19-Feb-15	Recovered/Resolved with sequelae	Not Related	Not Related
					4 cracked ribs (Rib fracture)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	17-Feb-15	19-Feb-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Laceration to her PPD (Skin laceration)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	17-Feb-15	19-Feb-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US017-1011	70-79 Year(s) Male		Myocardial infarction - non ST elevation (Acute myocardial infarction)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	10-Mar-15	11-Mar-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1116	70-79 Year(s) Female		Generalized weakness (Asthenia)	General disorders and administration site conditions	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Mar-15	10-Apr-15	Recovered/Resolved	Not Related	Not Related
					Visual hallucinations (Hallucination, visual)	Psychiatric disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Mar-15	13-Mar-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	AU005-1040	70-79 Year(s) Female		Colitis (Colitis)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	12-Mar-15	26-Mar-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Worsening of Rectal Prolapse (Rectal prolapse)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	10-Mar-15	11-Mar-15	Recovered/Resolved	Not Related	Not Related
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US063-1017	60-60-69 Year(s) Female		Shortness of breath (Dyspnoea)	Respiratory, thoracic and mediastinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15	12-Mar-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US013-1066	60-60-69 Year(s) Female		Congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15		Not Recovered/Resolved	Not Related	Not Related
					Pancreatitis (Pancreatitis)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15	18-Mar-15	Recovered/Resolved	Not Related	Not Related
					Accidental narcotic overdose (Accidental overdose)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15	18-Mar-15	Recovered/Resolved	Not Related	Not Related
					Metabolic encephalopathy (Metabolic encephalopathy)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15	18-Mar-15	Recovered/Resolved	Not Related	Not Related
					Acute renal failure (Acute kidney injury)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15	03-Jul-15	Recovered/Resolved	Not Related	Not Related
					Acute on chronic respiratory acidosis (Respiratory acidosis)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15		Not Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US012-1125	70-79 Year(s) Female		Diverticular disease (Diverticulum)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	04 Mar 2015		Not Recovered/Resolved	Not Related	Not Related
					Proximal colovesical fistula (Enterovesical fistula)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Mar 2015	18-Mar-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Pelvic abscess (Pelvic abscess)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Mar 2015	18-Mar-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US056-1001	70-79 Year(s) Male		Stroke (Cerebrovascular accident)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09 Mar 2015	09 Mar 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	US030-1095	70-79 Year(s) Female		Anuria (Anuria)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	21-Mar-15	21-Mar-15	Recovered/Resolved	Not Related	Not Related
					Bilateral obstructing ureteral stone (Ureterolithiasis)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	21-Mar-15	21-Mar-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US132-1002	60-69 Year(s) Female		Infectious gastroenteritis (Gastroenteritis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	27-Mar-15	11-Apr-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Fluzone Quadrivalent (11Feb15)	US032-1051	70-70-79 Year(s) Female		Allergic reaction (Hypersensitivity)	Immune system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	10-Mar-15	11-Mar-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US078-1072	80-89 Year(s) Female		Bilateral subdural hematoma (Subdural haematoma)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	02 Apr 2015	06-Apr-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US108-1073	60-69 Year(s) Female		Influenza A (Influenza)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	14-Apr-15	17-Apr-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US108-1021	80-89 Year(s) Female		Ataxia (Ataxia)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	12-Apr-15	13-Apr-15	Recovered/Resolved	Not Related	Not Related
					Accelerated Hypertension (Accelerated hypertension)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	12-Apr-15	13-Apr-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US079-1021	70-70-79 Year(s) Male		Pneumonia (Pneumonia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	16-Apr-15	16-May-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US073-1025	90 or older Year(s) Male	04 May 2015	Congestive heart failure (Cardiac failure congestive)	Cardiac disorders		SevereDeath	26-Apr-15	04 May 2015	Death	Not Related	Not Related
					Methicillin-sensitive staphylococcus aureus (MSSA) bacteremia secondary to cellulitis (Staphylococcal bacteraemia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Apr-15	04 May 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US029-1103	70-70-79 Year(s) Male		Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	20-Apr-15	01 May 2015	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1058	70-79 Year(s) Male		Diverticulitis (Diverticulitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	02 Apr 2015	05 Apr 2015	Recovered/Resolved	Not Related	Not Related
KLB-423880594	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US013-1086	80-89 Year(s) Female		MRSA cellulitis of PPD (Cellulitis staphylococcal)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26 Apr 2015	26 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Pneumonia (Pneumonia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	26 Apr 2015	10-May-15	Recovered/Resolved	Not Related	Not Related
					Sepsis (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26 Apr 2015	10-May-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (02Mar16)	US108-1046	80-89 Year(s) Male		Myocardial infarction (Myocardial infarction)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-May-16	15-May-16	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US063-1092	80-89 Year(s) Female		Appendicitis (Appendicitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	29-Apr-15	29-Apr-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US063-1058	60-69 Year(s) Female		Right lung metastatic carcinoma with gynecologic tract primary (Metastatic neoplasm)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Medically significant event	06 May 2015	30 Oct 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU006-1086	70-70-79 Year(s) Female		Stroke (Cerebrovascular accident)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	26-Mar-15	28-Mar-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US138-1037	70-79 Year(s) Female		Pulmonary embolism (Pulmonary embolism)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	15-Mar-15	22-Mar-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1046	60-69 Year(s) Female		Urosepsis (Urosepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	01 May 2015	02 Jun 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US017-1157	60-69 Year(s) Female		Worsening of right carotid cerebrovascular disease (Carotid artery disease)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	01 Apr 2015	06-Apr-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US030-1105	80-89 Year(s) Female		Chest pain (non-cardiac) (Non-cardiac chest pain)	General disorders and administration site conditions	Severe	In-patient hospitalisation;In-Patient Hospitalisation	12-Apr-15	12-Apr-15	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	US108-1040	70-79 Year(s) Female	22-Apr-15	Small cell carcinoma of lung (Small cell lung cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Death	02-Mar-15	22-Apr-15	Death	Not Related	Not Related
XSS-662341852	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US106-1051	70-79 Year(s) Female		PPD pain (Arthralgia)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	14-Apr-15	17-Apr-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Fluzone Quadrivalent (11Feb15)	US053-1061	70-70-79 Year(s) Male		Erosive duodenitis, erosive gastritis (Gastritis erosive)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	19-Mar-15	21-Mar-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US078-1072	80-89 Year(s) Female		Middle cerebral artery infarction (Cerebral infarction)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Apr-15	12-Apr-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	US108-1005	70-79 Year(s) Female		Coronary artery disease (Coronary artery disease)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	28-Apr-15	02 May 2015	Recovered/Resolved with sequelae	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US108-1057	70-79 Year(s) Female		Left upper lobe pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	13-Apr-15	15-Apr-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US108-1093	70-79 Year(s) Female		Acute ischemic stroke (Ischaemic stroke)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Apr-15	23-Apr-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US012-1136	70-79 Year(s) Male		Heart failure with preserved ejection fraction (Cardiac failure)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Apr-15	18-Apr-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Acute hypoxemic respiratory failure (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Apr-15	18-Apr-15	Recovered/Resolved with sequelae	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	US017-1027	60-69 Year(s) Female		Worsening of incisional hernia (Incisional hernia)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	12-Mar-15	26 Mar 2015	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US138-1087	80-89 Year(s) Male		Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	22-Mar-15	03-Apr-15	Recovered/Resolved	Not Related	Not Related
					Sepsis (Sepsis)	Infections and infestations	Moderate	Life threatening	22-Mar-15	25 Mar 2015	Recovered/Resolved	Not Related	Not Related
					Pleural effusions (Pleural effusion)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	22-Mar-15	02-Apr-15	Recovered/Resolved	Not Related	Not Related
					Acute hypoxia respiratory failure (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	24 Mar 2015	03-Apr-15	Recovered/Resolved	Not Related	Not Related
KLE-423980584	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US056-1057	60-69 Year(s) Male		Angina pectoris, unstable angina (Angina unstable)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08 May 2015	11-May-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Fluzone Quadrivalent (11Feb15)	AU001-1076	80-89 Year(s) Male		Community acquired pneumonia (Pneumonia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	29 Apr 2015	06-May-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US012-1094	80-89 Year(s) Female		Congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	09 May 2015		Not Recovered/Resolved	Not Related	Not Related
					Respiratory syncytial virus bronchiolitis (Respiratory syncytial virus bronchiolitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	09 May 2015	14-May-15	Recovered/Resolved with sequelae	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	US137-1062	60-69 Year(s) Male		Acute coronary syndrome (Acute coronary syndrome)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	16-Mar-15	18-Mar-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU005-1023	70-79 Year(s) Female		COPD with exacerbation (Chronic obstructive pulmonary disease)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 Apr 2015	02 May 2015	Recovered/Resolved	Not Related	Not Related
					Concern for aspiration pneumonia (Pneumonia aspiration)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 Apr 2015	02 May 2015	Recovered/Resolved	Not Related	Not Related
					Acute respiratory failure with hypoxia (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 Apr 2015	02 May 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US108-1065	70-79 Year(s) Female		Left lateral lung base pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	29 Apr 2015	02 May 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US138-1079	80-89 Year(s) Female		Acute anemia (Anaemia)	Blood and lymphatic system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-May-15	10-May-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	US071-1064	60-69 Year(s) Female		Community acquired pneumonia (Pneumonia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	13-May-15	18-May-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Fluzone Quadrivalent (11Feb15)	US056-1094	70-79 Year(s) Male		Atrial fibrillation with rapid ventricular rate (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Mar-15	02 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Mar-15		Not Recovered/Resolved	Not Related	Not Related
					Pulmonary embolism (Pulmonary embolism)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Mar-15	05 Dec 2015	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (10Feb16)	US066-1134	60-69 Year(s) Female		Congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Mar-16		Not Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					COPD exacerbation (Chronic obstructive pulmonary disease)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Mar-16	18-Mar-16	Recovered/Resolved	Not Related	Not Related
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US063-1042	60-69 Year(s) Female		Hiatal hernia (Hiatus hernia)	Gastrointestinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	31 Mar 2015	31 Mar 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU004-1013	60-69 Year(s) Female		Episode of temporary aphasia (Transient aphasia)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	15-May-15	18-May-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	US108-1026	70-79 Year(s) Female		Advanced arthritis PPD (Arthritis)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	12-May-15	12-May-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US079-1002	60-69 Year(s) Male		Worsening coronary artery disease (Coronary artery disease)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	08-May-15		Not Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US013-1066	60-69 Year(s) Female		MRSA cellulitis of PPD (Cellulitis staphylococcal)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27 May 2015	07-Jun-15	Recovered/Resolved	Not Related	Not Related
					Osteomylitis (Osteomyelitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27 May 2015	26 Jul 2015	Recovered/Resolved with sequelae	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US013-1086	80-89 Year(s) Female		Acute blood loss anemia (Blood loss anaemia)	Blood and lymphatic system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	21-May-15	29 May 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	US013-1091	70-79 Year(s) Male		Left carotid stenosis (Carotid artery stenosis)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Mar-15	25 Mar 2015	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1132	70-79 Year(s) Female		Acute bacterial pneumonia (Pneumonia bacterial)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03 Jun 2015	06 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Sepsis (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	03 Jun 2015	06 Jun 2015	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	AU006-1068	70-79 Year(s) Female		Atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	01 Jun 2015		Not Recovered/Resolved	Not Related	Not Related
XSS-662341852	Fluzone Quadrivalent (11Feb15)	US138-1160	80-89 Year(s) Female										

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Acute ischemic stroke (Ischaemic stroke)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	15-Jun-15	23-Jun-15	Recovered/Resolved with sequelae	Not Related	Not Related
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1116	70-79 Year(s) Female		Atrial fibrillation exacerbation (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jun-15	26-Jun-15	Recovered/Resolved	Not Related	Not Related
					Congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jun-15		Not Recovered/Resolved	Not Related	Not Related
					Shock liver (Ischaemic hepatitis)	Hepatobiliary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jun-15	26-Jun-15	Recovered/Resolved	Not Related	Not Related
					Rhabdomyolysis (Rhabdomyolysis)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jun-15	26-Jun-15	Recovered/Resolved	Not Related	Not Related
					Acute renal insufficiency (Acute kidney injury)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jun-15	26-Jun-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US063-1006	60-69 Year(s) Female		Appendicitis (Appendicitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	12-Jun-15	14-Jun-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	AU001-1063	80-89 Year(s) Female	25-May-15	Pneumonia (Pneumonia)	Infections and infestations	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation	23-May-15	25-May-15	Death	Not Related	Not Related
					Acute respiratory failure (Acute respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	23-May-15	25-May-15	Death	Not Related	Not Related
					Pulmonary embolism (Pulmonary embolism)	Respiratory, thoracic and mediastinal disorders	Severe	Death;Life threatening	23-May-15	25-May-15	Death	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	US108-1049	70-79 Year(s) Female		Benign cystic neoplasm of the left ovary (Benign ovarian tumour)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	01 Jul 2015	11-Jul-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	US013-1023	70-79 Year(s) Male		Cellulitis PPD (Cellulitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	05-Jul-15	14-Jul-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Osteomylitis (Osteomyelitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	09-Jul-15	14-Jul-15	Recovered/Resolved with sequelae	Not Related	Not Related
VOY-787346461	Fluzone Quadrivalent (11Feb15)	US106-1052	80-89 Year(s) Female		Influenza A (Influenza)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Jun 2015	26-Jun-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	AU006-2012	70-79 Year(s) Female		Gastrointestinal bleed (Gastrointestinal haemorrhage)	Gastrointestinal disorders	Mild	In-patient hospitalisation;In-Patient Hospitalisation	13-Jul-15	14-Jul-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US137-1088	70-70-79 Year(s) Female		Wound infection (Wound infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	30-Jun-15	07-Jul-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US132-1076	70-70-79 Year(s) Female		Worsening nodular goiter (Goitre)	Endocrine disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	06 May 2015	07 May 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1055	70-70-79 Year(s) Female		Aspiration pneumonia (Pneumonia aspiration)	Respiratory, thoracic and mediastinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	22-Jul-15	03 Aug 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	US017-1130	70-70-79 Year(s) Male		Subdural hematoma (Subdural haematoma)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	13-Jun-15	14-Jun-15	Recovered/Resolved with sequelae	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	US017-1130	70-70-79 Year(s) Male		Altered mental status (Mental status changes)	Psychiatric disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	24-Jul-15	01 Aug 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US132-1040	80-89 Year(s) Male		Septic cholecystitis (Cholecystitis infective)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	15-Jul-15	25-Jul-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1010	70-70-79 Year(s) Female		PPD intertrochanteric PPD fracture (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	06-Jul-15	11-Jul-15	Recovered/Resolved with sequelae	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US017-1008	60-69 Year(s) Female		Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Jul-15	30 Jul 2015	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	AU004-1004	70-79 Year(s) Female		Cardiac chest pain (Angina pectoris)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Jun-15	27-Jun-15	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US012-1121	60-69 Year(s) Male		Electrolyte dysfunction (Electrolyte imbalance)	Metabolism and nutrition disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	26-Mar-15	29-Mar-15	Recovered/Resolved	Not Related	Not Related
LBL-811783230	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US012-1121	60-69 Year(s) Male		Electrolyte dysturbance (Electrolyte imbalance)	Metabolism and nutrition disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	16-Apr-15	18-Apr-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Fluzone Quadrivalent (11Feb15)	US066-1038	60-69 Year(s) Female		Acute appendicitis w/o peritonitis (Appendicitis)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	09-May-15	12-May-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb16)	AU004-1024	70-70-79 Year(s) Female		Transient ischemic attack (Transient ischaemic attack)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	31 Jul 2016	02 Aug 2016	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US137-1093	70-70-79 Year(s) Female		PPD periprosthetic PP fracture (Periprosthetic fracture)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	01 Jul 2015	16-Aug-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	US013-1018	80-89 Year(s) Female	11-Jul-15	Diffuse subarachnoid hemorrhage (Subarachnoid haemorrhage)	Injury, poisoning and procedural complications	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	30 Jun 2015	11-Jul-15	Death	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	AU004-1050	70-79 Year(s) Female		Abdominal pain (Abdominal pain)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jun-15	12-Jul-15	Recovered/Resolved	Not Related	Not Related
					Duodenitis (Duodenitis)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jun-15	12-Jul-15	Recovered/Resolved	Not Related	Not Related
					Choledocholithiasis (Bile duct stone)	Hepatobiliary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jun-15	12-Jul-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (10Feb16)	AU006-3029	70-70-79 Year(s) Male		Right quadricep tendon tear (Tendon rupture)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	14-May-16	19-May-16	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	US018-1012	60-69 Year(s) Female		Colitis (Colitis)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Jun 2015	07-Jun-15	Recovered/Resolved	Not Related	Not Related
					Acute kidney injury (Acute kidney injury)	Renal and urinary disorders	Moderate	Medically significant event	04 Jun 2015	07-Jun-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Fluzone Quadrivalent (11Feb15)	US073-1066	70-79 Year(s) Female		Worsening of osteoarthritis of left hip (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	31 Mar 2015	18-Jul-15	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	US056-1043	60-69 Year(s) Female		Right breast cancer (Breast cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Medically significant event	01 Aug 2015	13-Nov-15	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Fluzone Quadrivalent (11Feb15)	AU004-1009	60-69 Year(s) Female		Cardiac chest pain (Angina pectoris)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	06 Aug 2015	07 Aug 2015	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US013-1051	70-79 Year(s) Female		Cellulitis of PPD (Cellulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 May 2015	01 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Viral enteritis (Gastroenteritis viral)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 May 2015	01 Jun 2015	Recovered/Resolved	Not Related	Not Related
					Sepsis secondary to group A Strep bacteremia (Streptococcal bacteraemia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 May 2015	01 Jun 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US066-1082	70-79 Year(s) Female	31 Jul 2015	Gastrointestinal bleeding (Gastrointestinal haemorrhage)	Gastrointestinal disorders	Severe	Death	29-Jul-15	31 Jul 2015	Death	Not Related	Not Related
					Liver cirrhosis (Hepatic cirrhosis)	Hepatobiliary disorders	Severe	Death	31 Jul 2015	31 Jul 2015	Death	Not Related	Not Related
					Hemorrhagic shock (Shock haemorrhagic)	Vascular disorders	Severe	Death	31 Jul 2015	31 Jul 2015	Death	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	US108-1044	60-69 Year(s) Female		Intracranial aneurysm (Intracranial aneurysm)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	05-Apr-15	19-Jun-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1050	80-89 Year(s) Male		Intracranial hemorrhage (Haemorrhage intracranial)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-May-15	28-May-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	AU001-1067	70-79 Year(s) Male		Non-ST elevated myocardial infarction (Acute myocardial infarction)	Cardiac disorders	Mild	In-patient hospitalisation;In-Patient Hospitalisation	28 Jun 2015	29 Jun 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US032-1043	80-89 Year(s) Male		COPD exacerbation (Chronic obstructive pulmonary disease)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26 Jun 2015	16-Jul-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Hypoxia (Hypoxia)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	02-Jul-15	02-Jul-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US138-1049	70-79 Year(s) Male		PPD distal PPD fracture (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17-May-15	16-Jul-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1074	70-79 Year(s) Male		PPD fracture (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-May-15	01 Jul 2015	Recovered/Resolved	Not Related	Not Related
					Nondisplaced PPD fracture (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-May-15	01 Jul 2015	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU006-3027	60-60-69 Year(s) Female		Broken PPD (PPD fracture)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	24-May-15	06-Dec-15	Recovered/Resolved	Not Related	Not Related
					Broken PPD (PPD fracture)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	24-May-15	06-Dec-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1029	80-89 Year(s) Male	05 Aug 2015	COVID-19 complications (COVID-19)	Infections and infestations	Severe	Death	05 Aug 2015	05 Aug 2015	Death	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	AU004-1002	70-79 Year(s) Female		Atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	17-Jun-15	18-Jun-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	US071-1052	70-79 Year(s) Female		Bowel obstruction (Intestinal obstruction)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-May-15	19-May-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU006-1021	70-79 Year(s) Female		PPD end-stage osteoarthritis (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	02-Jul-15	03-Jul-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US063-1012	70-79 Year(s) Male		Worsening HTN (Hypertension)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	09-Jul-15	10-Jul-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1084	60-69 Year(s) Female		Dehydration (Dehydration)	Metabolism and nutrition disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	02 Jun 2015	03-Jun-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1077	80-89 Year(s) Male		Post op pain (Procedural pain)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28 Jun 2015	01 Jul 2015	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	US017-1127	60-60-69 Year(s) Male		Myocardial infarction (Myocardial infarction)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Jun-15	24-Jun-15	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Fluzone Quadrivalent (11Feb15)	US066-1012	70-79 Year(s) Female		Urothelial carcinoma of kidney (Transitional cell carcinoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Jun-15	24-Jun-15	Recovered/Resolved with sequelae	Not Related	Not Related
LBL-811783230	Fluzone Quadrivalent (11Feb15)	US138-1123	70-79 Year(s) Male		Thyroid nodules follicular cancer (Follicular thyroid cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Disabled	29 Apr 2015	*	Not Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Lumbar/spine leiomyosarcoma (Leiomyosarcoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Disabled	07 May 2015		Not Recovered/Resolved	Not Related	Not Related
GCL-653380502	Fluzone Quadrivalent (11Feb15)	AU005-1050	70-79 Year(s) Female		PPD pain (Pain in extremity)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04 Apr 2015	10-Jun-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US138-1114	60-60-69 Year(s) Female		Endometrial cancer, stage 1 (Endometrial cancer stage I)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	Medically significant event	27 May 2015	05-Aug-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone Quadrivalent (11Feb15)	US079-1027	60-60-69 Year(s) Female		Worsening of osteoarthritis PPD (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	11-Mar-15	15-Oct-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US137-1003	70-79 Year(s) Male		Sepsis (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25 May 2015	31 May 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US017-1157	60-60-69 Year(s) Female		Worsening of aortic aneurysm (Aortic aneurysm)	Vascular disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Jun-15		Not Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US079-1040	60-69 Year(s) Female		Cerebrovascular accident (Cerebrovascular accident)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	04-Jun-15	08-Jun-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (13Aug15)	US012-1099	70-79 Year(s) Male	16-Feb-16	High grade partial small bowel obstruction (Small intestinal obstruction)	Gastrointestinal disorders	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	12-Feb-16	16-Feb-16	Death	Not Related	Not Related
					Acute diverticulitis (Diverticulitis)	Infections and infestations	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	12-Feb-16	16-Feb-16	Death	Not Related	Not Related
					Bilateral pneumonia (Pneumonia)	Infections and infestations	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	12-Feb-16	16-Feb-16	Death	Not Related	Not Related

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					Sepsis POA (Sepsis)	Infections and infestations	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event;Life threatening	12-Feb-16	16-Feb-16	Death	Not Related	Not Related
GCL-653380502	Fluzone Quadrivalent (11Feb15)	AU001-1051	70-79 Year(s) Female		Acute on chronic anemia (Anaemia)	Blood and lymphatic system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	04-Aug-15		Not Recovered/Resolved	Not Related	Not Related
					Acute abscess of left kidney (Renal abscess)	Infections and infestations	Moderate	Life threatening	22 Apr 2015	23 Sep 2015	Recovered/Resolved with sequelae	Not Related	Not Related
					Septic shock (Septic shock)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	05-Aug-15	15-Aug-15	Recovered/Resolved	Not Related	Not Related
					Recurrent left renal cell carcinoma (Renal cell carcinoma recurrent)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	Life threatening	22 Apr 2015	23 Sep 2015	Recovered/Resolved with sequelae	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US003-1081	60-69 Year(s) Female		Fall (Fall)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	05 Aug 2015	05 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Deep vein thrombosis (Deep vein thrombosis)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	05 Aug 2015	08-Aug-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU005-1012	80-89 Year(s) Female	27 Aug 2015	Blood clot (Thrombosis)	Vascular disorders	Severe	Death	27 Aug 2015	27 Aug 2015	Death	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	US132-1014	60-69 Year(s) Male		Pulmonary embolism (Pulmonary embolism)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	12-Sep-15	14-Sep-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	AU001-1051	70-79 Year(s) Female		Colo fistula (Colonic fistula)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Sep-15	23 Sep 2015	Recovered/Resolved	Not Related	Not Related
					Enterocutaneous fistula (Enterocutaneous fistula)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Sep-15	23 Sep 2015	Recovered/Resolved	Not Related	Not Related
					Abdominal fistula (Gastrointestinal fistula)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23 Sep 2015	01-Nov-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Acute bacterial pneumonia (Pneumonia bacterial)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26 Sep 2015	01-Nov-15	Recovered/Resolved	Not Related	Not Related
					Post-op intraabdominal abscess (Postoperative abscess)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	29-Sep-15	29-Sep-15	Recovered/Resolved	Not Related	Not Related

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					Septic shock (Septic shock)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	29-Sep-15	01-Nov-15	Recovered/Resolved	Not Related	Not Related
					Acute urinary tract infection (Urinary tract infection)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	10-Sep-15	19 Sep 2015	Recovered/Resolved	Not Related	Not Related
					Volume overload (Fluid overload)	Metabolism and nutrition disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	29-Sep-15	02-Oct-15	Recovered/Resolved	Not Related	Not Related
					Hyponatremia (Hyponatraemia)	Metabolism and nutrition disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	08-Sep-15	10-Oct-15	Recovered/Resolved	Not Related	Not Related
					Subarachnoid hemorrhage (Subarachnoid haemorrhage)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Sep-15	01-Nov-15	Recovered/Resolved	Not Related	Not Related
					Acute respiratory distress syndrome (Acute respiratory distress syndrome)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26 Sep 2015	01-Nov-15	Recovered/Resolved	Not Related	Not Related
					Acute hypoxemic respiratory failure (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	23 Sep 2015	23 Sep 2015	Recovered/Resolved	Not Related	Not Related
GCL-653380502	Fluzone Quadrivalent (11Feb15)	US078-1047	70-79 Year(s) Male		Leukocytosis (Leukocytosis)	Blood and lymphatic system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	11-Oct-15	17-Oct-15	Recovered/Resolved	Not Related	Not Related
					Stage IV Lung Cancer (Lung carcinoma cell type unspecified stage IV)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	03 Dec 2015		Not Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US132-1098	70-79 Year(s) Male		Community acquired pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	30 Aug 2015	23 Sep 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU004-1003	60-69 Year(s) Female		DVT to iliofemoral PP (Deep vein thrombosis)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	06-Aug-15	16-Sep-15	Recovered/Resolved with sequelae	Not Related	Not Related
UY0-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US017-1157	60-69 Year(s) Female	03 Sep 2015	Congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Severe	Death	03 Sep 2015	03 Sep 2015	Death	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US137-1093	70-79 Year(s) Female		Hypertensive urgency (Hypertensive urgency)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	16-Jun-15	19-Jun-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US108-1052	70-79 Year(s) Male		Diverticulitis (Diverticulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23-Nov-15	28-Nov-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1075	70-79 Year(s) Female		Estrogen-receptor positive breast cancer (Hormone receptor positive breast cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	Medically significant event	27-Oct-15	04 Dec 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US017-1077	80-89 Year(s) Male		PPD joint infection (Arthritis infective)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	30 Oct 2015	*	Not Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	US132-1035	70-79 Year(s) Female		Bulging disc (Intervertebral disc protrusion)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	30 Sep 2015	15-Jan-16	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	US012-1108	60-69 Year(s) Male		Acute fractures L1-L3, T5, T10 (Spinal fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17-Nov-15	10-Dec-15	Recovered/Resolved	Not Related	Not Related
					Acute fractures of PPD (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17-Nov-15	10-Dec-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1043	80-89 Year(s) Female	21-Nov-15	COVID 19 (COVID-19)	Infections and infestations	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation	13-Nov-15	21-Nov-15	Death	Not Related	Not Related
WEI-274448216	Fluzone Quadrivalent (11Feb15)	US017-1143	60-69 Year(s) Female		Renal failure (Renal failure)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	19-Nov-15		Not Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	US132-1070	80-89 Year(s) Male		Pancreatitis (Pancreatitis)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	01 Sep 2015	04 Sep 2015	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1082	70-79 Year(s) Female		PPD infection (Localised infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	20-Dec-15	02-Jan-16	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Fluzone Quadrivalent (11Feb15)	US132-1102	70-79 Year(s) Male		COVID-19 (COVID-19)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	30 Oct 2015	18-Nov-15	Recovered/Resolved with sequelae	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US135-1038	70-79 Year(s) Female		COVID-19 (COVID-19)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	06-Nov-15	18-Nov-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1045	80-89 Year(s) Female		Gastric ulcer (Gastric ulcer)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	20-Jan-16	23-Jan-16	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU004-1017	70-79 Year(s) Female		Transient ischemic attack (Transient ischaemic attack)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Oct-15	11-Oct-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU005-1006	80-89 Year(s) Female		Hiatus hernia (Hiatus hernia)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	06-Nov-15	09-Nov-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US066-1116	70-79 Year(s) Female	19-Sep-15	Death (Death)	General disorders and administration site conditions	Severe	Death	19-Sep-15	19-Sep-15	Death	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	US138-1134	70-79 Year(s) Male		Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Nov-15	13-Nov-15	Recovered/Resolved	Not Related	Not Related
					Sepsis (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Nov-15	13-Nov-15	Recovered/Resolved	Not Related	Not Related
					Acute kidney failure (Acute kidney injury)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	11-Nov-15	13-Nov-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Fluzone Quadrivalent (11Feb15)	US066-1026	80-89 Year(s) Male		Enlargement prostate (Prostatomegaly)	Reproductive system and breast disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18-Jan-16	19-Jan-16	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone Quadrivalent (11Feb15)	US063-1075	80-89 Year(s) Male		Worsening of torn labrum PPD (Cartilage injury)	Injury, poisoning and procedural complications	Moderate	Medically significant event	15-Oct-15	16-Oct-15	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US063-1080	90 or older Year(s) Male		Staph bacteremia (Staphylococcal bacteraemia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	28-Jan-16	13-Feb-16	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US050-1116	70-79 Year(s) Male		Herniated cervical disc (Intervertebral disc protrusion)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	11-Jan-16	15-Jan-16	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	US050-1140	80-89 Year(s) Female		Sick sinus syndrome (Sinus node dysfunction)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	21 Aug 2015	18-Dec-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1084	70-79 Year(s) Male		Worsening coronary artery disease (Coronary artery disease)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	29 Oct 2015	08-Nov-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1084	70-79 Year(s) Male		PPD ulcer infection (Infected skin ulcer)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	17-Nov-15	04-Dec-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU06-3027	80-89 Year(s) Male		SARS-COV-2 (COVID-19)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	21-Jan-16	01 Feb 2016	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone Quadrivalent (11Feb15)	AU006-1013	70-79 Year(s) Female		Gastrointestinal bleeding (Gastrointestinal haemorrhage)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	21-Sep-15	26 Sep 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	AU006-1009	70-79 Year(s) Female		Fractured vertebrae (Spinal fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	21-Nov-15	19-Dec-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU005-1059	70-79 Year(s) Female		Worsening of back pain (Back pain)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	05-Sep-15	05-Nov-15	Recovered/Resolved	Not Related	Not Related
KLB-423880584	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US137-1088	70-79 Year(s) Female		PPD laceration (Skin laceration)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	11-Jan-16	17-Jan-16	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Fluzone Quadrivalent (11Feb15)	US073-1081	60-69 Year(s) Female		Worsening osteoarthritis (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Mild	In-patient hospitalisation;In-Patient Hospitalisation	29-Dec-15		Not Recovered/Resolved	Not Related	Not Related
LBL-811783230	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1005	70-79 Year(s) Female		Blunt trauma to t PPce (PPD injury)	Injury, poisoning and procedural complications	Severe	Disabled;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved with sequelae	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
					Multisystem blunt trauma (Injury)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Multiple fractures (Multiple fractures)	Injury, poisoning and procedural complications	Severe	Disabled;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved with sequelae	Not Related	Not Related
					Motor vehicle collision (Road traffic accident)	Injury, poisoning and procedural complications	Severe	Disabled;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	13-Apr-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Left hemopneumothorax (Traumatic haemothorax)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Ischemic stroke (Ischaemic stroke)	Nervous system disorders	Severe	Disabled;In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Acute respiratory insufficiency (Acute respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Pulmonary insufficiency following trauma (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
					Deep vein thrombosis (Deep vein thrombosis)	Vascular disorders	Moderate	Life threatening	13-Apr-15	28 Apr 2015	Recovered/Resolved	Not Related	Not Related
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US079-1031	80-89 Year(s) Male		PPD fracture (PP fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	23 Oct 2015	03-Nov-15	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone Quadrivalent (11Feb15)	AU001-1021	70-70-79 Year(s) Male		Lung cancer (Lung neoplasm malignant)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Disabled;Medically significant event	25 Sep 2015	*	Not Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU002-1015	80-89 Year(s) Female		COVID-19 pneumonia (COVID-19 pneumonia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	01-Sep-15	11-Sep-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	AU005-1057	70-79 Year(s) Male		PPD pain (Arthralgia)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	30 Sep 2015	30 Sep 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	AU005-1057	70-79 Year(s) Male		Coronary artery disease (Coronary artery disease)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	06-Dec-15	13-Dec-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US030-1146	70-70-79 Year(s) Male		Transient global amnesia (Transient global amnesia)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	08-Jan-16	09-Jan-16	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US056-1034	70-70-79 Year(s) Female		Appendicitis (Appendicitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	05 Nov 2015	07 Nov 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU001-1032	60-69 Year(s) Male		Pneumonia (Pneumonia)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	22 Oct 2015	25 Oct 2015	Recovered/Resolved	Not Related	Not Related
					Sepsis with septic shock (Septic shock)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	22 Oct 2015	25 Oct 2015	Recovered/Resolved	Not Related	Not Related
					Encephalopathy (Encephalopathy)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	22 Oct 2015	25 Oct 2015	Recovered/Resolved	Not Related	Not Related
					Acute renal failure (Acute kidney injury)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	22 Oct 2015	25 Oct 2015	Recovered/Resolved	Not Related	Not Related
					Respiratory failure (Respiratory failure)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	22 Oct 2015	25 Oct 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	AU002-1022	80-89 Year(s) Female		Acute congestive heart failure (Cardiac failure congestive)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	09-Nov-15	11-Nov-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	US066-1024	70-79 Year(s) Female		Worsening of osteoarthritis PPD (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	07 Jan 2016	08-Jan-16	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US063-1043	70-70-79 Year(s) Female		Back pain (Back pain)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	27-May-15	30 May 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone Quadrivalent (11Feb15)	US106-1037	70-79 Year(s) Female	26-Oct-15	Myocardial infarction (Myocardial infarction)	Cardiac disorders	Severe	Death	26-Oct-15	26-Oct-15	Death	Not Related	Not Related
WEI-274448216	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US106-1033	70-79 Year(s) Female		Death (Death)	General disorders and administration site conditions	Severe	Death	07 Jan 2016	07 Jan 2016	Death	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Fluzone Quadrivalent (11Feb15)	US056-1100	70-79 Year(s) Female		COVID hospitalization (COVID-19)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	28 Sep 2015	* 27-Nov-15	* Recovered/Resolved	Not Related	Not Related
TKE-802742060	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US132-1043	80-89 Year(s) Female		Osteoarthritis exacerbation PPD (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	15-Mar-15	14-Oct-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Quad-NIV 240 µg+ Matrix-M1 75 µg (11Feb15)	US079-1031	80-89 Year(s) Male		PPD neck fracture (PPD neck fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	21-Nov-15	24 Nov 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Fluzone Quadrivalent (11Feb15)	US078-1074	70-79 Year(s) Male		Arterial spasm (Arterial spasm)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	16-Dec-15	18-Dec-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone Quadrivalent (11Feb15)	AU005-1024	70-79 Year(s) Female		Osteoarthritis (Osteoarthritis)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	05 Oct 2015	06-Oct-15	Recovered/Resolved	Not Related	Not Related

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Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
VOY-787546461	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (11Feb15)	US032-1056	70-79 Year(s) Female		Breast cancer in-situ duct carcinoma (Invasive ductal breast carcinoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Medically significant event	25 Feb 2015	30 Apr 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	RSV F nanoparticle 120µg + Aluminum phosphate (0.4 mg Al) (11Feb15; 04Mar15)	US045-1017	60-69 Year(s) Male		Septicemia (Sepsis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Mar-15	11-Mar-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	RSV F nanoparticle 120µg + Aluminum phosphate (0.4 mg Al) (11Feb15; 04Mar15)	US045-1025	60-69 Year(s) Female		Breast cancer (Breast cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	09-Mar-15		Not Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 95µg + Aluminum phosphate (0.3 mg Al) (11Feb15)	US045-1051	70-79 Year(s) Male		Bruising (Contusion)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	25-Mar-15	Recovered/Resolved	Not Related	Not Related
					Laceration PPD (Laceration)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	17 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Lacerations PPD (Laceration)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	26-Mar-15	Recovered/Resolved	Not Related	Not Related
					Laceration PPD (Laceration)	Injury, poisoning and procedural complications	Mild	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	17 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Fractured PPD (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	17 Aug 2015	Recovered/Resolved	Not Related	Not Related
					L3 spinal fracture (Spinal fracture)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	17 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Fractured sternum/ right 5th-9th rib (Sternal fracture)	Injury, poisoning and procedural complications	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	25-Feb-15	17 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Osteophyte impingement at C4/C5 (Vertebral osteophyte)	Musculoskeletal and connective tissue disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	25-Feb-15	12 Mar 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US050-1040	60-69 Year(s) Male		Infections and Infestations: Influenza A (Influenza)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17 Mar 2015	01-Apr-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1042	60-69 Year(s) Male		Acute arterial thrombus (Peripheral artery thrombosis)	Vascular disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	27-Mar-15	30-Mar-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	RSV F nanoparticle 95µg + Aluminum phosphate (0.3 mg Al) (11Feb15)	US044-1107	60-69 Year(s) Female		Connective tissue disease pneumonitis (Mixed connective tissue disease)	Musculoskeletal and connective tissue disorders	Severe	Disabled	26-Mar-15		Not Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 135µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1031	70-79 Year(s) Male		Possible cholecystitis (Cholecystitis)	Hepatobiliary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	10-Apr-15		Not Recovered/Resolved	Not Related	Not Related
TKE-802742060	RSV F nanoparticle 135µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1129	70-79 Year(s) Female		Atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	30-Mar-15	02-Apr-15	Recovered/Resolved with sequelae	Not Related	Not Related
HRV-151283347	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US032-1128	60-60-69 Year(s) Female		Mild sigmoid colon diverticulitis (Diverticulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04-May-15	07-May-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	RSV F nanoparticle 135µg (11Feb15; 04Mar15)	US044-1141	60-69 Year(s) Male		Type 2 Diabetes Mellitus (Type 2 diabetes mellitus)	Metabolism and nutrition disorders	Mild	Medically significant event	10-Jun-15		Not Recovered/Resolved	Not Related	Not Related
					Left corona radiata and inferior lentiform lacunar ischaemic stroke (Ischaemic stroke)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	10-Jun-15	26 Jun 2015	Recovered/Resolved with sequelae	Not Related	Not Related
IHG-548185183	RSV F nanoparticle 120µg + Aluminum phosphate (0.4 mg Al) (11Feb15; 04Mar15)	US045-1017	60-69 Year(s) Male		Worsened bladder neck narrowing (Bladder neck obstruction)	Renal and urinary disorders	Moderate	Medically significant event	28 Apr 2015	27 Jun 2015	Not Recovered/Resolved	Not Related	Not Related
VOY-787546461	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US032-1128	60-60-69 Year(s) Female		Clostridium difficile infection (Clostridium difficile infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	10-May-15	17 May 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US044-1021	60-60-69 Year(s) Male		Unstable angina (Angina unstable)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	02-Jul-15	04-Jul-15	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 135µg + Matrix-M1 (50µg) (11Feb15; 05Mar15)	US044-1132	60-69 Year(s) Male		Rhinovirus Respiratory Infection (Rhinovirus infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Jul-15	04 Aug 2015	Recovered/Resolved	Not Related	Not Related
					Exacerbation of COPD (Chronic obstructive pulmonary disease)	Respiratory, thoracic and mediastinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	26-Jul-15	04 Aug 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	RSV F nanoparticle 135µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1071	70-79 Year(s) Male		Malaena (Melaena)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	16-Sep-15	29 Sep 2015	Recovered/Resolved	Not Related	Not Related
					Gastric adenoma (Gastric adenoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	20-Sep-15	29 Sep 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1101	60-69 Year(s) Female		Influenza A (Influenza)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	15-Jun-15	18-Aug-15	Recovered/Resolved	Not Related	Not Related
					Lower respitatory tract infection (Lower respiratory tract infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	15-Jun-15	18-Aug-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	RSV F nanoparticle 120µg + Aluminum phosphate (0.4 mg Al) (11Feb15; 04Mar15)	US045-1030	60-69 Year(s) Male		Soft pansystolic heart murmur (Cardiac murmur)	Investigations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	19-Aug-15	29-Aug-15	Recovered/Resolved	Not Related	Not Related
					Worsening Bilateral Sciatica (Sciatica)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	19-Aug-15	29-Aug-15	Recovered/Resolved	Not Related	Not Related
					Mild hypoxia (Hypoxia)	Respiratory, thoracic and mediastinal disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	19-Aug-15	29-Aug-15	Recovered/Resolved with sequelae	Not Related	Not Related
IHG-548185183	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1067	70-79 Year(s) Female		Cholelithiasis (Cholelithiasis)	Hepatobiliary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	25-Jul-15	03 Oct 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	RSV F nanoparticle 135µg (11Feb15; 04Mar15)	US045-1132	70-79 Year(s) Male		Atrial Fibrillation (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	10 Sep 2015	01-Nov-15	Recovered/Resolved with sequelae	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 120µg + Aluminum phosphate (0.4 mg Al) (11Feb15; 05Mar15)	US044-1020	70-79 Year(s) Male		PPD ruptured tendon (Tendon rupture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17 Sep 2015	11-Jan-16	* Recovered/Resolved	Not Related	Not Related
TKE-802742060	RSV F nanoparticle 135µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US044-1110	80-89 Year(s) Male		Soft tissue injury PPD (Soft tissue injury)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	20 Jul 2015		Not Recovered/Resolved	Not Related	Not Related
HRV-151283347	RSV F nanoparticle 95µg + Aluminum phosphate (0.3 mg Al) (11Feb15; 04Mar15)	US045-1102	70-79 Year(s) Male	19 Oct 2015	Diverticular Disease (Diverticulum)	Gastrointestinal disorders	Severe	Medically significant event	23 Sep 2015		Not Recovered/Resolved	Not Related	Not Related
					Perforated bowel (Intestinal perforation)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	23 Sep 2015	30-Sep-15	Recovered/Resolved	Not Related	Not Related
					Peritoneal Metastatic Cancer- Unknown Primary (Malignant peritoneal neoplasm)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Death;Medically significant event	23 Sep 2015		Death	Not Related	Not Related
UYO-300644625	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US050-1031	60-60-69 Year(s) Male		Non-ST-elevation myocardial infarction (Acute myocardial infarction)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	12 Sep 2015	15 Sep 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US044-1135	60-69 Year(s) Male		SCC metastasis to parotid (Metastatic squamous cell carcinoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	18-Jul-15	14-Oct-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (15Feb15; 04Mar15)	US032-1076	70-79 Year(s) Male		Exacerbation of Congestive Heart Failure (Cardiac failure congestive)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	07-Oct-15	09-Jan-16	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US044-1021	60-60-69 Year(s) Male		Unstable angina (Angina unstable)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	30-Jan-16		Not Recovered/Resolved	Not Related	Not Related
					Headache (Headache)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	22-Dec-15	23-Mar-16	Recovered/Resolved	Not Related	Not Related
TKE-802742060	RSV F nanoparticle 135µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1120	60-60-69 Year(s) Male		Acute Myocardial Infarction (Acute myocardial infarction)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Life threatening	09-Feb-16	10-Feb-16	Recovered/Resolved	Not Related	Not Related
HRV-151283347	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US044-1135	60-69 Year(s) Male		Renal cell cancer grade 1 (Renal cancer stage I)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	23 Jun 2015	* 22-Mar-16	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Saline Placebo (11Feb15; 04Mar15)	US032-1055	70-79 Year(s) Female	11-Jan-16	Acute dissection of thoracic aorta (Aortic dissection)	Vascular disorders	Severe	Death	11-Jan-16	11-Jan-16	Death	Not Related	Not Related
IHG-548185183	Saline Placebo (11Feb15; 04Mar15)	US032-1071	70-79 Year(s) Male		Encephalitis (Encephalitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	24 Jan 2016		Not Recovered/Resolved	Not Related	Not Related
VOY-787546461	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US032-1076	70-79 Year(s) Male		Anaemia (Anaemia)	Blood and lymphatic system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	24 Jan 2016	30-Apr-16	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US032-1117	70-79 Year(s) Female		L5/S1 Disc Prolapse (Intervertebral disc protrusion)	Musculoskeletal and connective tissue disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	28-Sep-15	31-Dec-15	Recovered/Resolved with sequelae	Not Related	Not Related
					Radiculopathy (Radiculopathy)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	28-Sep-15	31-Dec-15	Recovered/Resolved with sequelae	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 120µg + Aluminum phosphate (0.4 mg Al) (11Feb15; 04Mar15)	US050-1001	70-79 Year(s) Female		Iron deficiency Anaemia (Iron deficiency anaemia)	Blood and lymphatic system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	24-Jul-15		Not Recovered/Resolved	Not Related	Not Related
TKE-802742060	RSV F nanoparticle 95µg + Aluminum phosphate (0.3 mg Al) (11Feb15; 05Mar15)	US050-1028	60-69 Year(s) Female		Influenza A (Influenza)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	23-Aug-15	26-Aug-15	Recovered/Resolved	Not Related	Not Related
					Haemophilus influenzae B pneumonia (Pneumonia haemophilus)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	23-Aug-15	26-Aug-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	RSV F nanoparticle 65µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1174	70-79 Year(s) Male		Coronary artery bypass stenosis (Coronary bypass stenosis)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	29-Oct-15	30-Oct-15	Recovered/Resolved with sequelae	Not Related	Not Related
UYO-300644625	RSV F nanoparticle 135µg (11Feb15; 04Mar15)	US044-1106	70-79 Year(s) Female		Hernia (Hernia)	General disorders and administration site conditions	Severe	In-patient hospitalisation;In-Patient Hospitalisation	22-Dec-15	26-Dec-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	RSV F nanoparticle 135µg (17Feb15; 10Mar15)	US044-1011	70-79 Year(s) Female		Progression of Meningioma (Meningioma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Disabled;In-patient hospitalisation;In-Patient Hospitalisation	11-Feb-15	12-Mar-15	Recovered/Resolved with sequelae	Not Related	Not Related
VOY-787546461	RSV F nanoparticle 35µg + Matrix-M1 (50µg) (11Feb15; 04Mar15)	US045-1104	60-69 Year(s) Female		Ganglioneuroma (Ganglioneuroma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	14 Nov 2015	16 Dec 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Saline Placebo (11Feb15; 06Mar15)	US044-1122	70-79 Year(s) Female		Left epiretinal membrane (Macular fibrosis)	Eye disorders	Severe	Medically significant event	15 Nov 2015	20 Feb 2016	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	RSV F nanoparticle 95µg + Aluminum phosphate (0.3 mg Al) (11Feb15; 04Mar15)	US045-1134	80-89 Year(s) Male		Cellulitis (Cellulitis)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	07-Mar-16	10-Mar-16	Recovered/Resolved	Not Related	Not Related

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Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
TKE-802742060	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 03Mar15)	US029-1098	60-69 Year(s) Male		Cerebral Vascular Accident (Cerebrovascular accident)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	28-Feb-15	02-Mar-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Fluzone HD (11Feb15; 03Mar15)	US018-1151	80-89 Year(s) Male		Group B Streptococcus (Beta haemolytic streptococcal infection)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	31-Mar-15	18 Apr 2015	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 05Mar15)	US018-1074	60-69 Year(s) Female		Chest tightness (Chest discomfort)	General disorders and administration site conditions	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	27-Feb-15	06-Mar-15	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone HD (11Feb15; 04Mar15)	US029-1013	70-79 Year(s) Male		Adenocarcinoma of Colon (Adenocarcinoma of colon)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	18 Mar 2015	18 Apr 2015	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Fluzone HD (11Feb15; 04Mar15)	US018-1073	70-79 Year(s) Male		Low grade papillary urothelial carcinoma (Bladder transitional cell carcinoma)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	21 Apr 2015	29-Apr-15	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 02Mar15)	US025-1016	70-79 Year(s) Female		PPD fracture (PPD fracture)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	20 May 2015	31-May-15	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 02Mar15)	US025-1016	70-79 Year(s) Female		Dislodgement of Titanium Shoulder (Device dislocation)	Product issues	Severe	In-patient hospitalisation;In-Patient Hospitalisation	09-Jun-15	16 Jul 2015	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US025-1026	60-69 Year(s) Male		Worsening of kidney stones (Nephrolithiasis)	Renal and urinary disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	19 May 2015	21 May 2015	Recovered/Resolved	Not Related	Not Related
TKE-802742060	Fluzone HD (11Feb15; 04Mar15)	US018-1041	60-69 Year(s) Female		Drug overdose (Overdose)	Injury, poisoning and procedural complications	Severe	In-patient hospitalisation;In-Patient Hospitalisation	17 Jul 2015	18 Jul 2015	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 03Mar15)	US025-1050	60-69 Year(s) Male		Stage 4 metastatic prostate cancer (Prostate cancer metastatic)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Medically significant event	30-May-15		Not Recovered/Resolved	Not Related	Not Related
UYO-300644625	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US029-1047	70-79 Year(s) Male		Lymphocytic colitis (Colitis microscopic)	Gastrointestinal disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	05-Aug-15		Not Recovered/Resolved	Not Related	Not Related
IHG-548185183	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US029-1009	60-69 Year(s) Female	17 Nov 2015	Gastric adenocarcinoma (Adenocarcinoma gastric)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	Death;In-patient hospitalisation;In-Patient Hospitalisation	18 Sep 2015	17 Nov 2015	Death	Not Related	Not Related
VOY-787546461	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US029-1009	60-69 Year(s) Female	17 Nov 2015	Leptomeningeal carcinomatosis (Metastases to meninges)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation	25-Oct-15	17 Nov 2015	Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Fluzone HD (11Feb15; 04Mar15)	US029-1014	70-79 Year(s) Male		Fever of unknown etiology (Pyrexia)	General disorders and administration site conditions	Severe	In-patient hospitalisation;In-Patient Hospitalisation	16 Oct 2015	19 Oct 2015	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Fluzone HD (11Feb15; 02Mar15)	US029-1040	70-79 Year(s) Male		Transient ischemic attack (Transient ischaemic attack)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	22-Sep-15	07-Oct-15	Recovered/Resolved with sequelae	Not Related	Not Related
KLB-423880584	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 03Mar15)	US029-1016	60-69 Year(s) Female		Seroma (Seroma)	General disorders and administration site conditions	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	28-Oct-15	28-Oct-15	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US018-1086	70-79 Year(s) Male		Prostate cancer (Prostate cancer)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Moderate	Medically significant event	25 Jul 2015	*	Not Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)
GCL-653380502	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US029-1009	60-69 Year(s) Female		Right lower lobe pneumonia (Pneumonia)	Infections and infestations	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	09-Nov-15		Not Recovered/Resolved	Not Related	Not Related
TKE-802742060	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 03Mar15)	US029-1099	60-69 Year(s) Male		Suprapubic abscess (Pelvic abscess)	Infections and infestations	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04-Nov-15	06-Nov-15	Recovered/Resolved	Not Related	Not Related
HRV-151283347	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US018-1042	60-69 Year(s) Male		Syncopal episode (Syncope)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	24-Oct-15	24-Oct-15	Recovered/Resolved	Not Related	Not Related
UYO-300644625	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US018-1068	70-79 Year(s) Female		Chest pain (Chest pain)	General disorders and administration site conditions	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	19 Sep 2015	21 Sep 2015	Recovered/Resolved	Not Related	Not Related
IHG-548185183	Fluzone HD (11Feb15; 04Mar15)	US018-1066	60-69 Year(s) Male		Persistent atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04-Nov-15	08-Nov-15	Recovered/Resolved	Not Related	Not Related
VOY-787546461	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 03Mar15)	US029-1098	60-69 Year(s) Male		Worsening of Cervical Radiculopathy (Cervical radiculopathy)	Nervous system disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation;Medically significant event	15 Dec 2015		Not Recovered/Resolved	Not Related	Not Related
JVQ-036087748	Tri-NIV 45 µg+ Matrix M1 50 µg (11Feb15; 04Mar15)	US018-1042	60-69 Year(s) Male		Atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	31-Dec-15	01-Jan-16	Recovered/Resolved	Not Related	Not Related
WEI-274448216	Fluzone HD (11Feb15; 02Mar15)	US029-1065	60-69 Year(s) Female		Pancreatic Adenocarcinoma (Adenocarcinoma pancreas)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Severe	In-patient hospitalisation;In-Patient Hospitalisation	18 Jan 2016		Not Recovered/Resolved	Not Related	Not Related
KLB-423880584	Fluzone HD (11Feb15; 04Mar15)	US018-1066	60-69 Year(s) Male		Persistent atrial fibrillation (Atrial fibrillation)	Cardiac disorders	Severe	In-patient hospitalisation;In-Patient Hospitalisation	04-Feb-16 *	07-Feb-16 *	Recovered/Resolved	Not Related	Not Related
XSS-662341852	Tri-NIV 180 µg+ Matrix M1 50 µg (11Feb15; 03Mar15)	US018-1088	60-69 Year(s) Male		Cerebrovascular accident (Cerebrovascular accident)	Nervous system disorders	Moderate	In-patient hospitalisation;In-Patient Hospitalisation	03-Jan-16	04-Jan-16	Recovered/Resolved	Not Related	Not Related

Case#	IP	Subject ID	Age Sex	Date of Death	SAE Verbatim (MedDRA PT)	MedDRA SOC	Severity	Serious Criteria	Onset Date (* approx)	End Date (* approx)	Outcome	Causality (Investigator)	Causality (Sponsor)

APPENDIX 2 NARRATIVES OF DEATHS, TREATMENT-RELATED SERIOUS ADVERSE EVENTS, AND IMPORTANT ADVERSE EVENTS OF SPECIAL INTEREST

9.1 Deaths

9.2 Treatment-Related Serious Adverse Events

9.3 Important Adverse Events of Special Interest

9.1 Deaths

There were a total of 24 deaths across the 5 Novavax-sponsored clinical trials of other recombinant nanoparticle vaccine antigens with Matrix-M1 adjuvant. Fourteen deaths occurred in participants who received Matrix-M1-adjuvanted vaccines, 8 deaths in participants who received active influenza vaccine comparator, 1 death in a participant who received placebo comparator, and 1 death in a participant who received a recombinant nanoparticle vaccine antigen without Matrix-M1 adjuvant. All reported deaths were assessed as not related to study treatment. All 24 deaths occurred in participants ≥ 65 years of age and were generally as expected for this age population and with participants' medical histories).

Subject number:	US045-1102
Subject demographics:	70-79-year-old White PPD male from PPD
Vaccine group:	RSV F nanoparticle 95µg + Aluminum phosphate (0.3 mg Al)
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	04 Mar 2015
Serious adverse events (SAEs):	Intestinal perforation Malignant peritoneal neoplasm Diverticulum
Death:	Malignant peritoneal neoplasm
Relationship of SAE/death to study vaccine:	Not related Not related Not related

Subject US045-1102 was a 70-79-year-old White PPD male from PPD. He experienced SAEs of intestinal perforation, malignant peritoneal neoplasm and diverticulum on 23 Sep 2015, after receiving both doses of RSV F nanoparticle 95 µg + aluminum phosphate (0.3 mg Al).

On 23 Sep 2015, 8 months after administration of the first dose of RSV F nanoparticle 95 µg + aluminum phosphate (0.3 mg Al) and 7 months after administration of the second dose, the subject went for a colonoscopy and endoscopy to investigate nausea and gastric bloating. The endoscopy showed the esophagus was normal with no evidence of esophageal varices; the stomach had a few erosions present in the gastric antrum; and the duodenum was normal; biopsies were taken for histology. The colonoscopy showed severe diverticular disease in the sigmoid colon with strictures. While trying to navigate the lower sigmoid colon, a bowel perforation occurred and the procedure was abandoned. The subject was admitted to the hospital and underwent an emergency laparoscopic Hartmann's procedure with peritoneal lavage, debridement of fibrin and division of adhesions to repair the perforated bowel. During the surgery, widespread malignancies were found in the peritoneum and biopsy samples were obtained. The bowel biopsies showed metastatic adenocarcinoma and immunostaining was CK7 positive and negative for PSA, CK20, CDX2 and TTF1. Chest x-ray showed cardio mediastinal outline appeared normal allowing for supine projection; mild peripheral peri-bronchial cuffing and some bibasilar linear atelectasis; and no acute pulmonary edema, pulmonary

collapse/consolidation or mass. On 24 Sep 2015, a chest x-ray showed clear lung fields, and no adverse features. On 30 Sep 2015, the subject was discharged from the hospital and the event of intestinal perforation was considered resolved. On an unspecified date in PPD the subject died. It was unknown if an autopsy was performed.

The Principal Investigator assessed the events as severe and not related to RSV F nanoparticle 95 µg + aluminum phosphate (0.3 mg Al). In the opinion of the Principal Investigator, the event of intestinal perforation was related to colonoscopy and the events of malignant peritoneal neoplasm and diverticulum were related to an unknown etiology. The Sponsor assessed the events of intestinal perforation, malignant peritoneal neoplasm and diverticulum as not related to RSV F nanoparticle 95 µg + aluminum phosphate (0.3 mg Al).

It is important to note that the subject had a past medical/surgical history significant for depression, and lower back pain. Concomitant medications included Celebrex, and sertraline.

Subject number:	US032-1055
Subject demographics:	70-79-year-old White PPD female from PPD
Vaccine group:	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	04 Mar 2015
Serious adverse event (SAE):	Aortic dissection
Death:	Aortic dissection
Relationship of SAE/death to study vaccine:	Not related

Subject US032-1055 was a 70-79-year-old White PPD female from PPD. She experienced an SAE of aortic dissection on 11 Jan 2016 after receiving both doses of placebo.

On 11 Jan 2016, 11 months after administration of the first dose of placebo and 10 months after administration of the second dose, the subject experienced acute dissection of the thoracic aorta. On 13 Jan 2016, the subject died at home due to a cardiac episode. The post-mortem findings per the autopsy report revealed the sac in which the heart was located was distended by blood, which had resulted from an acute dissection of the thoracic aorta towards its origin with a further area of splitting of the aortic wall within the thoracic cavity resulting in a left hemothorax. Marked pooling of fluid within the lungs was evident. No other gross pathology of significance was identified. The autopsy also found florid pulmonary edema, mild atherosclerosis and cholesterolosis of the gallbladder. Per the death certificate, the subject's cause of death was subject to examination of the heart. Per the coroner's autopsy report, the causes of death were listed as: 1a-hemopericardium and hemothorax and 1b- acute dissection of thoracic aorta.

The Principal Investigator assessed the event of aortic dissection as severe and not related to placebo. In the opinion of the Principal Investigator, the event of aortic dissection was potentially related to an unknown etiology. The Sponsor assessed the event of aortic dissection as not related to placebo.

It is important to note that the subject had a past medical history significant for coronary artery disease and was on no concomitant medications.

Subject number:	US029-1009
Subject demographics:	60-69-year-old White PPD female from the PPD
Vaccine group: first dose	Tri NIV 180 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Licensed seasonal Influenza vaccine
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	04 Mar 2015
Serious adverse event (SAE):	Adenocarcinoma gastric
Death:	Adenocarcinoma gastric
Relationship of SAE/death to study vaccine:	Not related

Subject US029-1009 was a 60-69-year-old White PPD female from the PPD She experienced an SAE of adenocarcinoma gastric on 18 Sep 2015 after receiving Tri-NIV 180 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and licensed seasonal influenza vaccine on 04 Mar 2015.

On 18 Sep 2015, 7 months after administration of Tri-NIV 180 µg + Matrix-M1 adjuvant 50 µg and 6 months after administration of a licensed seasonal influenza vaccine, the subject experienced adenocarcinoma gastric. The subject presented to the hospital with severe left sided abdominal pain, which started 2-3 months prior and worsened with inspiration and movement about six weeks ago. She had lost about PPD during this time and complained of a loss of appetite, nausea without vomiting and chronic diarrhea. She was admitted to the hospital for pain management and further work up. She was assessed by gastroenterology and diagnosed with irritable bowel syndrome (IBS). Diagnostic work up included a computed tomography (CT) of abdomen/pelvis without contrast that showed a large gastro-hepatic mass with multiple low attenuation hepatic lesions consistent with metastatic disease or lymphoma. CT pulmonary angiogram showed segmental atelectasis or scarring in the left lower lobe, no pulmonary edema or acute pulmonary embolism, with low attenuation lesions on the liver with a large gastro-hepatic mass attributed to metastatic disease and ascites. Chest x-ray showed atelectasis versus scar in the left lower lobe. On 20 Sep 2015, an upper gastrointestinal endoscopy showed a normal esophagus wall with a medium-sized, ulcerated, non-circumferential mass with no bleeding and no stigmata of recent bleeding found in the cardia. Biopsies confirmed gastric adenocarcinoma. Treatment included oral hydromorphone, Percocet, intravenous (IV) Fentanyl, and Lorazepam for pain, Enoxaparin for thrombosis prophylaxis, oral Protonix, and Zofran as needed for the gastro-hepatic mass. On 22 Sep 2015, the subject was discharged from the hospital. On 13 Oct 2015, the subject started chemotherapy treatment with 5FU and cisplatin. On 17 Nov 2015, the subject expired due to gastric adenocarcinoma gastric. An autopsy was not performed.

The Principal Investigator assessed the event of adenocarcinoma gastric as severe and not related to Tri-NIV 180 µg + Matrix-M1 adjuvant 50 µg. In the opinion of the Principal Investigator, the event of adenocarcinoma gastric was potentially related to an unknown etiology. The Sponsor assessed the event of adenocarcinoma gastric as not related to Tri-NIV 180 µg + Matrix-M1 adjuvant 50 µg.

It is important to note the subject had a medical history significant for ocular hypertension, hyperlipidemia, glaucoma, and tobacco dependence on one half pack of cigarettes a day. Concomitant medications included brimonidine tartrate, Lipitor, and timolol.

Subject number:	US029-1139
Subject demographics:	70-79-year-old White male PPD male from the PPD
Vaccine group: first dose	Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	26 Jun 2015
Date of second dose of study vaccine:	22 Jul 2015
Serious adverse events (SAEs):	Lung cancer metastatic Syncope Failure to thrive Dehydration Hypokalaemia
Death:	Lung cancer metastatic
Relationship of SAE/death to study vaccine:	Not related Not related Not related Not related Not related

Subject US029-1139 was a 70-79-year-old White male PPD male from the PPD He experienced SAEs of lung cancer metastatic on 30 Jun 2015, syncope on 23 Oct 2015, failure to thrive, dehydration, and hypokalemia on 03 Nov 2015 after receiving Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg on 26 Jun 2015 and placebo on 22 Jul 2015.

On 11 Feb 2015, prior to randomization, the subject was PPD . Diagnostic test results included trans-thoracic echocardiogram, which showed an ejection fraction of 62%. Pulmonary function tests showed moderate obstructive lung disease. Lung volume measurement showed mild restrictive lung disease. Magnetic resonance imaging (MRI) of the head showed several small old infarcts and no acute intracranial abnormality. Carotid ultrasound showed right internal carotid artery (ICA) with severe occlusive disease and left internal carotid artery with moderate occlusive disease. He was treated with ketorolac and Kenalog injections.

On 30 Jun 2015, 4 days after administration of Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg, the subject was diagnosed with right lung cancer, metastatic to bone and brain. On 23 Oct 2015, 17 weeks after administration of Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg and 13 weeks after administration of placebo, the subject experienced syncope, and on 03 Nov 2015, 18 weeks after administration of Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg and 14 weeks after administration of placebo, the subject experienced failure to thrive, dehydration, and hypokalemia. Computerized tomography angiography (CTA) of the neck showed significant carotid stenosis (70%) in the right ICA, an azygos lobe mass was noted on the right measuring 3.2 cm, evidence of mediastinal, right hilar and right lower cervical lymphadenopathy suggestive of lung cancer. After the CTA, the subject PPD . He was taken to the emergency department (ED). CT scan of the head without contrast was negative for any acute fracture or hemorrhage. An electrocardiogram

(ECG) showed normal sinus rhythm, rate of 67 and QTc of 424. A chest x-ray obtained due to altered mental status showed no active disease. A CT of the chest with contrast showed a 3.5 × 2.5 × 3.9 centimeter right azygos lobe bronchogenic neoplasm with associated right hilar, right para-tracheal, low cervical lymphadenopathy and two indeterminate hepatic lesions. The subject was released from the ED the same day. On 08 Jul 2015, PET CT revealed a hyper-metabolic lesion in the medial right upper chest, possibly involving both the azygos lobe of the lung and the adjacent mediastinum with at least one liver metastasis and findings suspicious for metastasis in the right sixth rib, right femur, and possibly C7. On 15 Jul 2015, the subject had a bronchoscopy with a biopsy, which revealed non-small cell carcinoma consistent with adenocarcinoma. On 11 Aug 2015, the subject started chemotherapy with Alimta/carboplatin/ Keytruda with close subsequent follow of the brain lesion. The subject was to receive Zometa every 3 weeks for the metastatic disease involving the bone. In addition, the subject received Neulasta to prevent a decline in white blood cell count (WBC). After receipt of the first chemotherapy cycle, the subject developed a fever and was hospitalized. A sepsis work-up was negative. He continued to receive chemotherapy and additional diagnostic tests showed metastatic disease. He was hospitalized several times for progressive symptoms of metastasis and hospice services were initiated. On 23 Nov 2015, the subject passed away. The death certificate noted metastatic lung cancer as the immediate cause of death.

The Principal Investigator assessed the events of lung cancer metastatic, syncope, failure to thrive, dehydration, and hypokalemia as severe and not related to Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg or placebo. In the opinion of the Principal Investigator, the events of lung cancer metastatic, syncope, failure to thrive, dehydration, and hypokalemia were potentially related to unknown etiology. The Sponsor assessed the events of lung cancer metastatic, syncope, failure to thrive, dehydration, and hypokalemia as not related to Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg or placebo.

It is important to note the subject had a medical history significant for elevated cholesterol, transient ischemic attack, diabetes mellitus type 2, hypertension, asthma, prior myocardial infarction, chronic obstructive pulmonary disease, ex-smoker for PPD (stopped PPD Dec2011) and currently drank alcohol but denied illicit drug use. Concomitant medications included Lipitor, Protonix, Adalat, Invokana, Plavix, ASA, metoprolol, Imdur, Singulair, Tricor, Cozaar, Humalog, Breo Ellipta, Pro Air, Deltasone, Voltaren gel, Cymbalta, and nitroglycerin.

Subject number:	US029-1006
Subject demographics:	60-69-year-old White PPD female from the PPD
Vaccine group: first dose	Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	11 Mar 2015
Serious adverse event (SAE):	Aortic aneurysm rupture
Death:	Cardiopulmonary collapse Hypovolemic shock Thoracic aortic aneurysm
Relationship of SAE/death to study vaccine:	Not related Not related Not related Not related

Subject US029-1006 was a 60-69-year-old White PPD female from the PPD She experienced SAE of aortic aneurysm rupture on 20 Jun 2015 after receiving Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and placebo on 11 Mar 2015.

On 18 Jun 2015, the subject presented to in-patient care for a one-day history of lower back and left abdominal pain; associated symptoms included nausea, non-bloody emesis, and non-bloody diarrhea. Physical examination included blood pressure of 164/125 mmHg, heart rate of 88, respiratory rate of 14, and oxygen saturation of 98% on 2 liters of oxygen. Her presentation was consistent with dehydration given elevated lactate and minimal urine production. A CT of the chest/abdomen/pelvis showed increase in size of the thoracic aortic aneurysm. On 20 Jun 2015, 4 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 3 months after administration of placebo, the subject experienced thoracoabdominal aneurysm and died. When the physician arrived at the bedside, the subject was found to be unresponsive with pulseless electrical activity rhythm, emesis from the mouth, and a mildly distended abdomen. Attempts at resuscitation were unsuccessful and the subject was diagnosed with a presumed aortic rupture in hemorrhagic shock. Life support efforts were stopped and the subject was pronounced dead. The death certificate noted cardiopulmonary collapse, hypovolemic shock, and thoracic aortic aneurysm as immediate causes of death. An autopsy was not performed.

The Principal Investigator assessed the event of aortic aneurysm rupture as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or placebo. In the opinion of the Principal Investigator, the event of aortic aneurysm rupture was potentially related to thoracic aortic aneurysm. The Sponsor assessed the event of aortic aneurysm rupture as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or placebo

It is important to note the subject had a medical history significant for hyperlipidemia, hypertension, thoracic aortic aneurysm, aortic aneurysm repair, and a prior history of cigarette smoking. Concomitant medications included Aspirin, atorvastatin, and metoprolol.

Subject number:	US004-1009
Subject demographics:	80-89-year old White PPD male from the PPD
Vaccine group: first dose	Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	11 Mar 2015
Serious adverse events (SAEs):	Respiratory failure Small intestinal obstruction Pulmonary embolism
Death:	Respiratory failure Pulmonary embolism
Relationship of SAEs/death to study vaccine:	Not related Not related Not related

Subject was an 80-89-year old White PPD male from the PPD. He experienced SAEs of small intestinal obstruction on 07 May 2015, respiratory failure and pulmonary embolism on 13 May 2015 after receiving Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and placebo on 11 Mar 2015.

On 02 May 2015, the subject presented to the emergency room (ER) after experiencing the sudden onset of lower abdominal pain for 30 minutes after eating fried food and felt cramping and moderate pain in the upper abdominal area. A computerized tomography (CT) scan of abdomen and pelvis without contrast showed increased reticular densities in the lung bases with bronchial wall thickening suggesting bronchitis, a normal appendix, no evidence of dilated bowel, dilated bowel thickening, diverticulitis or abnormal fluid in the large or small bowel. There was cholelithiasis and bilateral nephrolithiasis with no hydronephrosis or ureteral calculus. The subject was diagnosed with cholelithiasis and was discharged to home on the same day. On 05 May 2015, the subject presented to his primary care physician (PCP) as he had been vomiting black material. He had generalized weakness, abdominal pain with no bowel movement for 2 days, nausea and lack of appetite. Vital signs included temperature of 97.6 degrees F, heart rate 68, respiratory rate 18 and blood pressure 72/44. He was diagnosed with hematemesis, hypotension and dehydration and was instructed to proceed to the ER due to hypotension and coffee ground emesis. Examination revealed abdominal tenderness (diffuse) with guarding and rebound. Vital signs included temperature 97.8 degrees F, pulse rate 106, respiratory rate 18, and blood pressure 83/52, pulse oximetry 94%. CT of the abdomen and pelvis without contrast showed small bowel obstruction with transition point in the right lower quadrant, bilateral non obstructive nephrolithiasis measuring up to 5 mm of left, pulmonary nodules 8 mm in the lingual and right lower lobe, cholelithiasis, and a prior aorto iliac bypass graft with a calcified 3 cm aneurysm involving the left common iliac artery. Chest x-ray showed no acute process. Ultrasound of the kidneys showed normal sized kidneys without obstruction, and a moderate sized left renal cyst. ECG showed possible abnormal left atrial enlargement, sinus tachycardia, increased ventricular rate, and lengthened QT. The subject was placed on 2 liters of oxygen via nasal cannula and started on empiric antibiotics of Rocephin and Flagyl for intra-abdominal

source. His blood pressure improved (124/63) after IV fluids. The primary admission diagnosis was small bowel obstruction. The surgical consult noted that the subject did not require urgent surgical intervention; a likely source was some sort of enteritis and the acute renal failure was secondary to vomiting and diarrhea. The plan was to follow the subject daily until return of bowel function. On 06 May 2015, the subject had no complaints of nausea or vomiting. He appeared confused but was alert and awake in no acute distress. The subject's vital signs included temperature 37.4 degrees C, pulse 88, respiration 20, and blood pressure 118/71. The subject had decreased breath sounds at the bases (on 2 L oxygen by nasal cannula) with no distress; distended abdomen, tympanic to percussion with hypoactive bowel sounds; the subject has not had a bowel movement. The subject was continued on antibiotics; antihypertensive medication and Lasix were placed on hold.

On 07 May 2015, 85 days after administration of Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg and 57 days after administration of placebo, the subject experienced small bowel obstruction and on 13-May-2015, 91 days after administration of Quad-NIV 300 µg + Matrix-MI 50 µg and 63 days after administration of placebo, the subject experienced hypoxic hypercapnic respiratory failure and pulmonary embolism. He looked chronically ill, was confused but alert, and oriented x 2. He had no flatus or bowel movement. Examination revealed distended abdomen, tympanic to percussion with hypoactive bowel sounds, and decreased breath sounds at bases (on 2 L oxygen by nasal cannula). His presentation and findings were noted to be consistent with small bowel obstruction with no associated infection. Chest x-ray revealed tracheal tube residing 6.7 cm above the carina, interval placement of a right internal jugular central venous catheter with tip in the right atrium, development of bibasilar air space opacities, which may show single or a combination of atelectasis, aspiration, or infection. Abdominal x-ray revealed findings consistent with persistent high-grade partial small bowel obstruction. The subject underwent exploratory laparotomy, lysis of adhesions, and placement of right ileo jejunal (IJ) triple lumen for small bowel obstruction. Operative findings included adhesions, distended small bowel with point of obstruction in the right lower quadrant with the loop of bowel that was in the pelvis. The subject tolerated the procedure well, was kept intubated and taken to the ICU in guarded condition. On 09 May 2015, the subject was transferred from the ICU to the floor. He still had no flatus or bowel movements. A chest x-ray showed improved aeration of the left lung base, minimal left pleural effusion minimal right pleural effusion, and mild pulmonary vascular congestion, unchanged. The subject's oxygen saturation was in the 90s with oxygen via nasal cannula. On 10 May 2015, the subject had increased work of breathing, was placed on Bipap due to hypoxemia, and was moved from the floor to the PCU. Chest x-ray revealed patchy opacities at the right lung base, which could indicate pneumonia, pneumonitis or sub-segmental atelectasis. Abdominal x-ray revealed multiple dilated loops of small bowel, small amount of stool in the hepatic flexure, high-grade partial small bowel obstruction; the impression was early versus partial small bowel obstruction. On 12 May 2015, the subject experienced worsening of respiratory status and tachycardia (pulse rate 118 -183) overnight. Arterial blood gases showed pH 7.430, pC02 38.0, p02 121, C02 26.4. CT of the abdomen and pelvis without contrast showed probable postoperative ileus again and could not exclude mechanical bowel obstruction. Chest x-ray showed no evidence of active cardiopulmonary disease. Ventilation perfusion (VQ) scan showed large ventilation perfusion defects in the superior segment left lower lobe and lingular segment left upper lobe and small defects in the dependent right lower lobe. The combination of these findings was consistent with high probability for pulmonary embolism (PE). ECG showed probable atrial tachycardia, non-specific ST and T wave abnormality, ST depression in anterior

leads, non-specific T wave abnormality evident in inferior leads. A transthoracic echocardiogram revealed mildly reduced left ventricular systolic function, an ejection fraction of 35% to 40%, possible hypokinesis of the mid apical anterior, mid anteroseptal and apical wall, and the aorta. An exploratory laparotomy and lysis of adhesions was performed for early post-op small bowel obstruction with distal adhesions. The subject was started on heparin drip on an unspecified date.

On 13 May 2015, an ultrasound of the lower extremities arterial duplex showed occlusion of the popliteal artery and all 3 tibial runoff vessels with no flow detected below the knee; there was an incidental acute deep vein thrombosis (DVT) within the left common femoral vein. Chest x-ray showed mild bibasilar atelectasis, no pneumothorax and an unchanged cardiac silhouette. The subject's status was changed to "do not resuscitate". The subject's family requested withdrawal of endotracheal tube and the subject was pronounced dead at 16:20. The causes of death were hypoxic hypercapnic respiratory failure and pulmonary embolism, due to complications during surgery to correct small bowel obstruction. No autopsy was performed.

The Principal Investigator assessed the events of small bowel obstruction, respiratory failure, and pulmonary embolism as severe and not related to Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg or placebo. In the opinion of the Principal Investigator, the events of respiratory failure and pulmonary embolism were potentially related to complications from surgery and the event of small bowel obstruction was potentially related to sepsis. The Sponsor assessed the events of small bowel obstruction, respiratory failure, and pulmonary embolism as not related to Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg or placebo.

It is important to note the subject had a medical history significant for chronic obstructive pulmonary disease, hypertension, coronary artery disease with chronic systolic heart failure, , hyperlipidemia, cerebrovascular accident, myocardial infarction, pulmonary fibrosis of right lung, abdominal aortic aneurysm repair, ex-smoker, upper extremity deep vein thrombosis, and hypertension. Concomitant medications included Prilosec, Coreg, simvastatin, lisinopril, Norvasc, albuterol, Lasix, MiraLAX, nitroglycerin, Trelegy, Aspirin, and loperamide.

Subject number:	US025-1127
Subject demographics:	80-89-year-old White PPD female from the PPD
Vaccine group: first dose	Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	10 Mar 2015
Serious adverse events (SAEs):	Cerebral arteriosclerosis Dementia Alzheimer's type Ischaemic cerebral infarction
Death:	Cerebral atherosclerosis
Relationship of SAEs/death to study vaccine:	Not related Not related Not related Not related

Subject US025-1127 was an 80-89-year-old White PPD female from the PPD . She experienced SAEs of cerebral arteriosclerosis and ischemic cerebral infarction on 05 Jun 2015, Dementia Alzheimer's type on 16 Jun 2015 after receiving Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and placebo on 10 Mar 2015.

On 05 Jun 2015, 16 weeks after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 12 weeks after administration of placebo, the subject experienced cerebral atherosclerosis and acute ischemic left middle cerebral artery (MCA) stroke and on 16 Jun 2015, 17 weeks after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 13 weeks after administration of placebo, the subject experienced late onset of Alzheimer's disease. She was admitted to the ER due to slurred speech. Upon admission, she was found to have right sided weakness and aphasia. Diagnostic tests included a head CT scan that showed a large, ill-defined area of subcortical/cortical hypodensity throughout the left temporal and parietal lobes, suspicious for acute or subacute left MCA territory ischemia/infarction; a neck CT scan showed abrupt occlusion of a left MCA M2 segment at the anterior left Sylvian fissure region; and a head MRI also identified the acute left MCA territory infarct with hemorrhagic transformation. While hospitalized, the subject experienced an episode of twitching and Keppra was initiated. O 12Jun2015 the subject was discharged to a skilled nursing facility. On 15 Jun 2015, the subject experienced intermittent agitation, lethargic episodes, bilateral lower extremity petechial rash, recurrent non-bloody vomiting, and decreased oral intake. On 16 Jun 2015, she was transferred back to the hospital. Head CT scan showed decreased edema associated with the subacute left MCA territory infarct. She was diagnosed with late onset Alzheimer's disease without behavioral disturbance. Diagnostic tests included a chest x-ray that showed increased bi-basal atelectasis reflecting aspiration or pneumonia. Head MRI showed expected evolution of MCA infarct without evidence of significant extension with nearly completely resolved hemorrhagic component and small right parietal infarct; this was also seen in the head CT scan. On 22 Jun 2015, the subject was discharged to home hospice with Augmentin to treat pneumonia and Zofran to treat recurrent vomiting. On 09 Jul 2015, the subject died while in hospice care. A

death certificate noted cerebral atherosclerosis as the immediate cause of death. No autopsy was performed.

The Principal Investigator assessed the events of cerebral arteriosclerosis, ischemic cerebral infarction and dementia Alzheimer's type as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or placebo. In the opinion of the Principal Investigator, the events of cerebral arteriosclerosis, ischemic cerebral infarction and dementia Alzheimer's type were potentially related to an unknown etiology. The Sponsor assessed the events of cerebral arteriosclerosis, ischemic cerebral infarction and dementia Alzheimer's type as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or placebo.

It is important to note the subject had a medical history significant for hypertension, hypercholesterolemia, atrial fibrillation, chronic kidney disease, and dementia. Concomitant medications included carvedilol, amlodipine, pravastatin, aspirin, and lisinopril.

Subject number:	AU006-2015
Subject demographics:	70-79-year-old White PPD male from the PPD
Vaccine group: first dose	Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	12 Mar 2015
Serious adverse events (SAEs):	Respiratory failure Acute myocardial infarction
Death:	Respiratory failure
Relationship of SAEs/death to study vaccine:	Not related Not related

Subject AU006-2015 was a 70-79-year-old White PPD male from the PPD He experienced SAEs of acute myocardial infarction on 18 May 2015 and respiratory failure on 02 Jun 2015 after receiving Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and placebo on 12 Mar 2015.

On 18 May 2015, 3 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 2 months after administration of placebo, the subject experienced acute non-ST-segment elevation myocardial infarction and on 02 Jun 2015, 3 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 2 months after administration of placebo, the subject experienced hypoxemic respiratory failure. On 18 May 2015, the subject was admitted to the hospital for heart problems, had a quadruple bypass, and never woke up from surgery. On 18 May 2015, the event of acute non-ST-segment elevation myocardial infarction was considered resolved. On 02 Jun 2015, the subject was taken off life support and expired. Per the death certificate, the immediate cause of death was hypoxemic respiratory failure as a consequence of acute non-ST segment elevation myocardial infarction; chronic tobacco use was noted as the underlying cause.

The Principal Investigator assessed the events of acute myocardial infarction and respiratory failure as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or Placebo. In the opinion of the Principal Investigator, the event of acute myocardial infarction was potentially related to coronary artery disease and the event of respiratory failure was potentially related to chronic tobacco use. The Sponsor assessed the events of acute myocardial infarction and respiratory failure as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or Placebo.

It is important to note the subject had a medical history significant for hypertension and coronary artery disease. Concomitant medication included lisinopril.

Subject number:	US106-1080
Subject demographics:	60-69-year-old White PPD female from the PPD
Vaccine group: first dose	Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	13 Mar 2015
Serious adverse event (SAE):	Death
Death:	Unknown
Relationship of SAE/death to study vaccine:	Not related

Subject US106-1080 was a 60-69-year-old White PPD female from the PPD She died on 26 Apr 2015 after receiving Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and placebo on 13 Mar 2015.

On 24 Mar 2015, the subject was hospitalized for an unspecified reason and was discharged from the hospital on 07 Apr 2015. On 26 Apr 2015, 10 weeks after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 6 weeks after administration of placebo, the subject was found deceased in her apartment. The subject did not have family or children and emergency contact information did not contain a phone number; therefore, the death certificate and cause of death were unobtainable. It was unspecified whether or not an autopsy was performed.

The Principal Investigator assessed the event of death as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or Placebo. In the opinion of the Principal Investigator, the event of death was potentially related to an unknown etiology. The Sponsor assessed the event of death as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg or Placebo.

It is important to note the subject had a medical history significant for coronary artery disease, type 2 diabetes, chronic renal insufficiency, anxiety, depression and hypertension. Concomitant medications included bupropion, Losartan, Humalog and aspirin.

Subject number:	US108-1054
Subject demographics:	60-69-year-old White PPD male from the PPD
Vaccine group: first dose	Flublok Quadrivalent
Vaccine group: second dose	Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of second dose of study vaccine:	11 Mar 2015
Serious adverse event (SAE):	Road traffic accident
Death:	Road traffic accident
Relationship of SAE/death to study vaccine:	Not related

Subject TK180-2742 was a 60-69-year-old White PPD male from the PPD. He died from a road traffic accident on 19 Mar 2015 after receiving Flublok Quadrivalent on 11 Feb 2015 and placebo on 11 Mar 2015.

On 19 Mar 2015, 5 weeks after administration of Flublok Quadrivalent and 8 days after administration of placebo, the subject died from a motor vehicle accident. PPD No autopsy was performed. A death certificate was unobtainable.

The Principal Investigator assessed the event of road traffic accident as severe and not related to Flublok Quadrivalent or Placebo. In the opinion of the Principal Investigator, the event of road traffic accident was potentially related to motor vehicle accident. The Sponsor assessed the event of road traffic accident as not related to Flublok Quadrivalent or Placebo.

It is important to note the subject had a medical history significant for hypertension, and generalized body pain. Concomitant medications included felodipine, enalapril hydrochlorothiazide, Tylenol, naproxen, and albuterol.

Subject number:	US066-1029
Subject demographics:	80-89-year-old White PPD male from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	COVID-19
Death:	COVID-19 complications
Relationship of SAE/Death to study vaccine:	Not related

Subject US066-1029 was an 80-89-year-old White PPD male from the PPD He died due to an SAE of COVID-19 on 05 Aug 2015 after receiving his single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

On 05 Aug 2015, 5 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject died from COVID-19 complications. At the time of death, he was in physical and chemical restraints and in isolation (enhanced droplet and contact) due to COVID-19. His code status was "Do Not Resuscitate" (DNR). The site noted that due to not having the proper medical release form signed by the subject, the expiration summary was all the hospital disclosed to the site. On 05 Aug 2015, the outcome of the event was death.

The Principal Investigator assessed the event of COVID-19 as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of COVID-19 was potentially related to the subject's underlying medical conditions of asthma and COPD. The Sponsor assessed the event of COVID-19 as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a medical/surgical history significant for angina pectoris, coronary artery disease, asthma, chronic obstructive pulmonary disease, gastroesophageal reflux disease, atrial fibrillation, cardiac ablation, symptomatic seasonal allergies, myocardial infarction, and stent placement. Concomitant medications included citalopram, albuterol, Trelegy Ellipta, ibuprofen, loratadine, nitroglycerin, acetaminophen, magnesium, and Eliquis.

Subject number:	US066-1116
Subject demographics:	70-79-year-old White PPD female from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Death
Death:	Death (Unknown)
Relationship of SAE to study vaccine:	Not related

Subject US066-1116 was a 70-79-year-old White PPD female from the PPD She experienced an SAE of death on 19 Sep 2015 after receiving her single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

On 19 Sep 2015, 7 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject experienced death due to an unknown cause. It was unknown if an autopsy was performed.

The Principal Investigator assessed the event of death as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of death was potentially related to an unknown etiology. The Sponsor assessed the event of death as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a past medical history significant for post-menopausal, atrial fibrillation, depression, back pain, bilateral knee pain (degenerative joint disease), insomnia, obesity, osteoarthritis bilateral knees, anxiety, hypertension, and obstructive sleep apnea. Concomitant medications included atenolol, Cymbalta, Percocet, temazepam, warfarin, acetaminophen, Xanax, trazodone, and morphine.

Subject number:	US106-1033
Subject demographics:	70-79-year-old White PPD female from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Death
Death:	Undetermined cause of death
Relationship of SAE/Death to study vaccine:	Not related

Subject US106-1033 was a 70-79-year-old White PPD female from the PPD She died on 07 Jan 2016 after receiving her single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

On 07 Jan 2016, 11 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject passed away at home. The death certificate noted the cause of death was undetermined. An autopsy was not performed.

The Principal Investigator assessed the event of death as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of death was potentially related to an underlying medical condition. The Sponsor assessed the event of death as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a past medical history significant for gastroesophageal reflux, anxiety, peripheral edema, hypertension, type 2 diabetes, hyperlipidemia, streptomycin allergy, generalized osteoarthritis, and dyspnea. Concomitant medications included omeprazole, paroxetine, furosemide, metoprolol, ramipril, glipizide, simvastatin, Ventolin, and Tylenol.

Subject number:	US132-1043
Subject demographics:	80-89-year-old White PPD female from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	COVID-19
Death:	Acute hypoxic respiratory failure COVID-19
Relationship of SAE to study vaccine:	Not related

Subject US132-1043 was an 80-89-year-old White PPD female from the PPD. She experienced an SAE of COVID-19 on 13 Nov 2015 after receiving her single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

Prior to the event, in PPD the subject experienced an exacerbation of PPD arthritis and was admitted to the hospital for hip replacement surgery. On an unspecified date post-operatively, she was discharged to a rehabilitation facility.

On 13 Nov 2015, 9 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject was admitted to the hospital with a diagnosis of COVID-19. On 21 Nov 2015, the event resulted in death. An autopsy was not performed. Per the death certificate, the causes of death were acute hypoxic respiratory failure and COVID-19.

The Principal Investigator assessed the event of COVID-19 as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of COVID-19 was potentially related to COVID-19. The Sponsor assessed the event of COVID-19 as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a past medical/surgical history significant for atrial fibrillation, hepatitis B antibody, increased creatinine, diabetes type II, hypercholesterolemia, diabetic neuropathy, osteoarthritis, back pain, back surgery, and hypertension. Concomitant medications included amiodarone, lisinopril, Eliquis, Januvia, rosuvastatin, Tylenol Arthritis, and hydrocodone/acetaminophen 5/325.

Subject number:	AU005-1012
Subject demographics:	80-89-year-old White PPD female from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Thrombosis
Death:	Blood clot
Relationship of SAE to study vaccine:	Not related

Subject AU005-1012 was an 80-89-year-oldWhite PPD female from the PPD She experienced an SAE of thrombosis on 27 Aug 2015 and died after receiving her single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

On 27 Aug 2015, 6 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject was rushed to the hospital and died. The cause of death was reported as blood clot; the location of the thrombosis was not known.

The Principal Investigator assessed the event of thrombosis as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of thrombosis was potentially related to an unknown etiology. The Sponsor assessed the event of thrombosis as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a past medical history significant for hypertension, gout left foot, depression, hypercholesterolemia, muscle spasm, and osteoarthritis in fingers. Concomitant medications included lisinopril, Lipitor, allopurinol, Celexa, amlodipine, and Flexeril.

Subject number:	US003-1030
Subject demographics:	70-79-year-old Other PPD male from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse events (SAEs):	Hepatic cirrhosis Complication associated with device
Death:	Complication associated with device
Relationship of SAEs/Death to study vaccine:	Not related Not related

Subject US003-1030 was a 70-79-year-old Other not Hispanic or PPD male from the PPD He experienced SAEs of hepatic cirrhosis on 11 Feb 2015 and complication associated with device on 15 Feb 2015 after receiving his single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

On 11 Feb 2015, on the day of administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject's pre-administration vital signs included blood pressure of 118/73 mmHg, temperature 36.4 degrees Celsius, respiration rate 16 breaths per minute, and heart rate 78 beats per minute. The subject received Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg at 09:23. Post-administration, his vital signs included blood pressure of 135/86, temperature 36.5°C, respiration rate 16 breaths per minute, and heart rate 81 beats per minute. At 16:00, approximately 6-7 hours after the administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject presented to the ER complaining of abdominal pain, nausea, and vomiting that started that afternoon and a loose bowel movement that occurred only the day before. An abdominal computerized tomography (CT) showed liver cirrhosis with ascites and a large right-sided pleural effusion with compressive atelectasis. In the ER, his vital signs were stable, and he was treated with 1 L of IV normal saline, pantoprazole, fentanyl, and Zofran. Abnormal laboratory data included hemoglobin of 12.1 (low), hematocrit 39.9 (low), RDW 16.9 (high), immature granulocyte percentage 0.5% (high), neutrophil percentage (auto) 86.3%, absolute lymphocyte count 0.47 (low), segmented neutrophil percentage 89% (high), monocyte percentage 1% (low), PT 15.4 (high), creatinine 1.4 (high), estimated GFR (MDRD) 50 (low), estimated GFR (CKD-EPI) 49 (low), glucose 156 (high), AST 10 (low), alkaline phosphatase 253 (high), albumin 3.2 (low) (units and reference ranges not provided). Despite treatment, the subject continued to feel unwell and was subsequently transferred to another facility for bowel rest and gastrointestinal (GI) evaluation. On 12 Feb 2015, peritoneal fluid was collected which was straw colored and clear; RBC was <2000/µL, nucleated cells 357/µL, neutrophils 12.0%, lymphocytes 52%, macrophages 26%, mesothelial cells 10%, total protein 4.3 g/d, and albumin 2.1 g/dL. On 14 Feb 2015, another sample of peritoneal fluid was collected; the culture showed no growth at Day 5. On 15 Feb 2015, the subject was discharged from the hospital.

On 15 Feb 2015, 4 days after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject experienced cardiac stent collapse (complication associated with device). Later that day, the subject collapsed on his way to his car and became unresponsive; he had pulseless electrical activity (PEA) and received epinephrine chest compressions. In the ER, the subject had

intermittent runs of ventricular tachycardia. Amiodarone bolus pulse drip was initiated controlled his irregular rhythm. The subject was intubated but his oxygenation remained difficult to maintain; arterial blood gases (ABG) revealed poor oxygenation and O2 saturations were in the mid-80s. A chest x-ray revealed marked cardiomegaly, right-sided defibrillator, and sternal sutures, but no heart failure, pneumonia, or pleural effusion. ABGs showed pH at 7.25 (7.35 - 7.45), ABG pO2 18 mmHg (75 – 100). An EKG revealed atrial fibrillation and right bundle branch block; a heparin bolus and drip were initiated. The subject was assessed in cardiac arrest with intermittent ventricular tachycardia, and severe ischemic cardiomegaly. He later died the same day. Cause of death was cardiac stent collapse (complication associated with device). No death certificate or autopsy were available.

The Principal Investigator assessed the event of hepatic cirrhosis as moderate and the event of complication associated with device as severe and both events as not related to the Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of hepatic cirrhosis was related to an unknown etiology and the event of complication associated with device was potentially related to coronary artery disease. The Sponsor assessed the events of hepatic cirrhosis and complication associated with device as not related to the Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a past medical/surgical history significant for hypertension, hypercholesterolemia, ischemic cardiomyopathy, chronic atrial fibrillation, combined systolic and diastolic congestive heart failure, coronary artery disease with 2 cardiac stents placed in PPD previous coronary artery bypass grafting (3 vessels), cirrhotic liver disease, recurrent ascites, stage III chronic kidney disease, and smoking (former smoker). He had an automatic cardioverter/defibrillator. Concomitant medications included lisinopril, atorvastatin, clopidogrel, amiodarone, and aspirin.

Subject number:	US017-1157
Subject demographics:	60-69-year-old White PPD female from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Cardiac failure congestive
Death:	Cardiac failure congestive
Relationship of SAE to study vaccine:	Not related

Subject US017-1157 was a 60-69-year-old White PPD female from the PPD . She experienced an SAE of cardiac failure congestive and died on 03 Sep 2015 after receiving her single dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

On 03 Sep 2015, 6 months after administration of Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg, the subject experienced cardiac failure congestive and died. Per the death certificate, the cause of death was congestive heart failure; an autopsy was not performed.

The Principal Investigator assessed the event of cardiac failure congestive as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg. In the opinion of the Principal Investigator, the event of cardiac failure congestive was potentially related to the underlying medical condition of coronary artery disease. The Sponsor assessed the event of cardiac failure congestive as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 75 µg.

It is important to note that the subject had a past medical/surgical history significant for myocardial infarction, hyperlipidemia, back osteoarthritis, hypertension, cerebrovascular disease, nicotine patch adhesive allergy, carotid artery repair-stent placed left side, carotid artery stent placed, abdominal aortic aneurysm, left carotid stenosis, right carotid stenosis, and coronary artery disease. Concomitant medications included aspirin, atorvastatin, baclofen, metoprolol, multivitamins, iron, vitamin B12, magnesium, lisinopril, amlodipine, cetirizine, and Plavix.

Subject number:	US066-1082
Subject demographics:	70-79-year-old White PPD female from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse events (SAEs):	Gastrointestinal haemorrhage Shock haemorrhagic Hepatic cirrhosis
Death:	Haemorrhagic shock
Relationship of SAEs/Death to study vaccine:	Not related Not related Not related

Subject US066-1082 was a 70-79-year-old White PPD female from the PPD . She experienced SAEs of gastrointestinal hemorrhage on 29 Jul 2015, hepatic cirrhosis and shock hemorrhagic on 31 Jul 2015 after receiving her single dose of 2019-20 Fluzone Quadrivalent.

On 09 Jul 2015, the subject had a total knee arthroplasty and had been on Mobic, Norco, and aspirin while at a Sub-Acute Rehab (SAR). On 29 Jul 2015, 5 months after administration of 2019-20 Fluzone Quadrivalent, the subject presented to the ED with hematemesis × 2 and vomiting. She had no prior history of gastrointestinal bleeding and was not on oral anticoagulant for atrial fibrillation. She was admitted to the intensive care unit for close hemodynamic monitoring. COVID-19 evaluation was started. Laboratory test results showed hemoglobin 10.2, hematocrit 30.5, platelets 132, lymphocytes relative 13.7, monocytes relative 12.8, lymphocytes absolute 1.0, monocytes absolute 0.9 and eosinophils absolute 0.40 (units and reference range not provided). Comprehensive metabolic panel results included abnormal findings for sodium 125, chloride 93, glucose 138, BUN 28 (reference ranges and units not provided), calcium 7.3 mg/dl (8.4-10.2), total protein 5.3 g/dl (6.3-8.2), albumin 2.1 g/dl (3.5-5), AST 41 U/L (14-36), total bilirubin 2.4 mg/dl (0.2-1.3), anion gap 9 (10-20), BUN/creatinine ration 35 (12-20), Albumin/globulin ratio 0.7 (1.1-2.2). Additional abnormal results included Prothrombin time 19.3, INR 1.77, PTT 39 (reference ranges and units not provided) and occult blood in stool. . The subject was given IV pantoprazole 80 mg in sodium chloride 0.9%. On 30 Jul 2015, no hematemesis was noted. Abnormal laboratory test result findings showed an increase in total bilirubin from the previous day (9.5 mg/dl). She was moved to IMCU for performance of the EGD. The subject had electrolyte abnormalities and the EGD was put on hold. The rapid response team was called for massive hematemesis. She was found minimally responsive with agonal respirations, SpO_2 in the 80s, and was noted with bright red emesis and melanotic stool. She was transferred to the ICU and intubated. Chest x-ray showed patchy airspace opacities, most notable in the right upper lobe and left lung base, suspicious for atypical pneumonia. An ECG showed wide QRS, left axis deviation, and left bundle branch block. An ultrasound liver spleen Doppler showed a large volume of ascites, hepatic cirrhosis, and increased renal cortical echotexture seen in the setting of chronic medical renal disease. Ultrasound guided paracentesis yielded 4000 ml of clear ascitic fluid. Shortly after intubation, the subject had a cardiac arrest

with return of spontaneous circulation after two rounds of epinephrine. The family changed her code status to DNR. On 31 Jul 2015 at 0621, the subject died. Immediate cause of death was hemorrhagic shock with contributing factors of gastrointestinal bleeding and liver cirrhosis.

The Principal Investigator assessed the events of gastrointestinal hemorrhage, shock hemorrhagic, and hepatic cirrhosis as severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the events of gastrointestinal hemorrhage and shock hemorrhagic were potentially related to an unknown etiology and the event of hepatic cirrhosis was potentially related to the underlying medical condition of cirrhosis. The Sponsor assessed the events of gastrointestinal hemorrhage, shock hemorrhagic, and hepatic cirrhosis as not related to 2019-20 Fluzone Quadrivalent.

It is important to note that the subject had a past medical history significant for hypertension, obesity, cirrhosis of liver, and chronic obstructive pulmonary disease. Concomitant medications included meloxicam, metoprolol, fluticasone/salmeterol, furosemide, brimonidine, Ventolin HFA, lactulose, and rifampin.

Subject number:	US073-1025
Subject demographics:	90 or older-year-old White PPD male from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse events (SAEs):	Cardiac failure congestive Staphylococcal bacteraemia
Death:	Congestive heart failure
Relationship of SAEs/ Death to study vaccine:	Not related Not related

Subject US073-1025 was a 90 or older-year-old White PPD male PPD . He experienced SAEs of cardiac failure congestive and Staphylococcal bacteremia on 26 Apr 2015 after receiving his single dose of 2019-20 Fluzone Quadrivalent.

On 26 Apr 2015, 10 weeks after administration of 2019-20 Fluzone Quadrivalent, the subject was hospitalized with cellulitis of legs secondary to a fall. He presented to the ER with a history of falling while walking to his bathroom 2-3 days prior. The next day, he noticed his PPD PPD felt painful and began to swell, then his PPD PPD hurt and began to swell as well. The subject also hurt his solar plexus and was mildly short of breath. Examination revealed his PPD PPD to be erythematous with 3+ doughy pitting edema, mildly tender, warm skin with no weeping. His PPD PPD was non-erythematous with 2+ pitting edema, mildly tender, and warm. A bilateral lower extremity venous Doppler ultrasound showed no evidence of thrombus. An ECG revealed normal sinus rhythm with 1st degree A-V block with premature ventricular or aberrantly conducted complexes left axis deviation, right bundle branch block, left ventricular hypertrophy with repolarization abnormality, possible lateral infarct (age undetermined). The subject had a known ejection fraction of 25-30% as of Jun2018. Clindamycin was initiated every 8 hours for cellulitis of legs. The subject's chronic anemia required no intervention. His resuscitation status was a Do Not Resuscitate (DNR) and he wanted less invasive treatment, understanding that it may affect his hospital course. On 27 Apr 2015, a chest x-ray performed due to chest pain on inspiration showed no acute pulmonary disease. During the hospitalization, the subject was found to have Methicillin-sensitive Staphylococcus aureus (MSSA) bacteremia secondary to cellulitis, which was initially treated with Daptomycin, and later switched to Ancef. On an unspecified date, the subject expressed his desire to receive palliative care only. Daptomycin and Ancef was discontinued. On the morning of 04 May 2015, the subject was released from the hospital to hospice care and died later in the day. The cause of death was congestive heart failure. The death certificate noted the manner of death as natural cause; the immediate cause of death was congestive heart failure due to coronary heart disease. An autopsy was not performed. The event of Staphylococcal bacteremia secondary to cellulitis was considered resolved. The event of cardiac failure congestive resulted in death.

The Principal Investigator assessed the events of cardiac failure congestive and Staphylococcal bacteremia as severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the event of cardiac failure congestive was related to coronary artery disease and the event of Staphylococcal bacteremia was potentially related to MSSA cellulitis.

The Sponsor assessed the events of cardiac failure congestive and Staphylococcal bacteremia as not related to 2019-20 Fluzone Quadrivalent.

It is important to note that the subject's past medical/surgical history was significant for congestive heart disease, chronic kidney disease, anemia, hyperlipidemia, hypertension, atrial fibrillation, coronary artery disease, myocardial infarction, allergy to penicillin, and contrast dye. Concomitant medications included simvastatin, aspirin, isosorbide mononitrate, metoprolol, and spironolactone.

Subject number:	US106-1037
Subject demographics:	70-79-year-old White PPD female from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Myocardial infarction
Death:	Myocardial infarction
Relationship of SAE/Death to study vaccine:	Not related

Subject US106-1037 was a 70-79-year-old White PPD female from the PPD. She experienced an SAE of myocardial infarction on 26 Oct 2015 after receiving her single dose of 2019-20 Fluzone Quadrivalent.

On 26 Oct 2015, 8 months after administration of 2019-20 Fluzone Quadrivalent, the subject passed away suddenly from a myocardial infarction. Cause of death was myocardial infarction. Per the site, no further information was available as the subject's PPD was unwilling to provide the autopsy report or death certificate.

The Principal Investigator assessed the event of myocardial infarction as severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the event of myocardial infarction was potentially related to an underlying medical condition. The Sponsor assessed the event of myocardial infarction as not related to 2019-20 Fluzone Quadrivalent.

It is important to note that the subject had a past medical history significant for hyperlipidemia and anxiety. Concomitant medications included fenofibrate and sertraline.

Subject number:	US108-1040
Subject demographics:	70-79-year-old White PPD female from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Small cell lung cancer
Death:	Small cell lung cancer
Relationship of SAE/Death to study vaccine:	Not related

Subject US108-1040 was a 70-79-year-old White PPD female from the PPD. She experienced an SAE of small cell lung cancer on 02 Mar 2015 after receiving her single dose of 2019-20 Fluzone Quadrivalent.

On 02 Mar 2015, 19 days after the receipt of 2019-20 Fluzone Quadrivalent, the subject had been feeling unwell for the prior 6 weeks and was referred to a pulmonologist. A chest x-ray showed a 4-centimeter lung mass. On an unspecified date, the subject presented to the site for her Day 28 appointment and appeared thin and sounded hoarse. On 24 Mar 2015, the subject had a lung biopsy. On 27 Mar 2015, the subject informed the clinical site staff of the small cell lung cancer diagnosis. On 22 Apr 2015, the subject died from small cell lung cancer.

The Principal Investigator assessed the event of small cell lung cancer as severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the event was potentially related to an unknown etiology. The Sponsor assessed the event of small cell lung cancer as not related to 2019-20 Fluzone Quadrivalent.

It is important to note that the subject's past medical/surgical history was significant for depression and current smoker. Concomitant medications included Lamictal and Seroquel.

Subject number:	AU001-1063
Subject demographics:	80-89-year-old White PPD female from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse events (SAEs):	Acute respiratory failure Pulmonary embolism Pneumonia
Death:	Acute respiratory failure
Relationship of SAEs/Death to study vaccine:	Not related Not related Not related

Subject AU001-1063 was an 80-89-year-oldWhite PPD female from the PPD . She experienced SAEs of acute respiratory failure, pulmonary embolism, and pneumonia on 23May2015 after receiving her single dose of 2019-20 Fluzone Quadrivalent.

On 23 May 2015, 3 months after administration of 2019-20 Fluzone Quadrivalent, the subject experienced acute respiratory failure, pulmonary embolism, and pneumonia. On 24 May 2015, per the subject's PPD, the subject's lung cancer returned. On 25 May 2015, the subject died. An autopsy was not performed. The cause of death was acute respiratory failure per the Death Certificate.

The Principal Investigator assessed the events of acute respiratory failure, pulmonary embolism, and pneumonia as severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the events of acute respiratory failure, pulmonary embolism, and pneumonia were potentially related to the underlying medical condition of lung cancer stage III adenocarcinoma. The Sponsor assessed the events of acute respiratory failure, pulmonary embolism, and pneumonia as not related to 2019-20 Fluzone Quadrivalent.

It is important to note that the subject had a past medical history significant for hypertension, hypothyroidism, acid reflux, pneumonia, and right lung cancer in remission. Concomitant medications included omeprazole, atenolol, amlodipine, and furosemide.

Subject number:	US012-1099
Subject demographics:	70-79-year-old White PPD male from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse events (SAE):	Small intestinal obstruction POA Sepsis Diverticulitis Pneumonia
Death:	High grade partial small bowel obstruction
Relationship of SAEs to study vaccine:	Not related Not related Not related Not related

Subject US012-1099 was a 70-79-year-old White PPD male from the PPD . He experienced SAEs of small intestinal obstruction, POA Sepsis, diverticulitis, and pneumonia on 12 Feb 2016 after receiving his single dose of 2019-20 Fluzone Quadrivalent.

On 12 Feb 2016, 6 months after administration of 2019-20 Fluzone Quadrivalent, the subject presented to the ER with intermittent diarrhea, vomiting, abdominal distension, and abdominal pain of 9 days duration. He was admitted and a computerized tomography (CT) of abdomen and pelvis was concerning for a life threatening small intestinal obstruction with focal wall thickening and adjacent punctate foci of extraluminal air that was concerning for micro-perforation. Chest x-ray was negative. WBC morphology showed vacuolated neutrophils present (abnormal). A transthoracic echocardiogram showed estimated ejection fraction 60-65%, no regional wall motion abnormalities, left atrium severely dilated, very mild aortic stenosis, mild to moderate tricuspid regurgitation, trace pulmonic regurgitation, and no pericardial effusion. Abnormal laboratory results included WBC 25.1, sodium 132, potassium 3.0, creatinine 1.44, lactic acid level 1.2, Troponin <0.02 negative x1, INR not detectable and APTT greater than 103 critical (units and reference range not provided). Tests for C. difficile stool, and urine culture were negative; blood culture had no growth. On 13 Feb 2016, neutrophils were 89.9 (high) and lymphocytes 2.6 (low), lactic acid level 1.3 (units and reference range not provided). On 14 Feb 2016, he underwent exploratory laparotomy with lysis of adhesion, ventral hernia repair and insertion of mesh. PT 11.4 and INR 1.05 (units and reference range not provided). Treatment included IV Reglan, Flagyl, meropenem, antifungal and Daptomycin. He had acute respiratory failure/ hypoxia, with pneumonia, minimal pulmonary embolus, in the setting of post-surgical, increased oxygen demand which was treated with Vapotherm, one time dose of Lasix IV and morphine IV to decrease air hunger and respiratory rate. CTA chest showed moderate right and mild to moderate left lower lobe pneumonia with minimal PE; heparin drip was started. CT of the head was negative. Cardizem drip continued. On 15 Feb 2016, WBC 27.3 (high), absolute neutrophils 25.39 (high), absolute lymphocytes 0.55 low, absolute monocytes 1.37 high, segmented neutrophils 92 high, lymphocytes 2 low, RBC morphology showed toxic granulation (slight abnormal). B type Natriuretic peptide 370.2 high, PT high at 12.6, INR 1.17, C reactive

protein (CRP) 10.1 high. Serum electrolytes and renal function test results were within normal limits except for chloride 113 high, BUN 25 high. Albumin 2.3 low, total protein 6.3 low, globulin 4.0 high, alkaline phosphatase 256 high, magnesium 3.0 high (units and reference range not provided). Arterial blood gases showed pH 7.47 high, pCO2 41, pO2 102 high, base excess 5.6 high, bicarbonate 29.2 high, Carboxyhgb 2.3, oxygen saturation of 95%. On 16 Feb 2016, WBC 26.1 high, absolute neutrophils 22.9 high, absolute lymphocytes 0.6 low, absolute monocytes 2.5 high, neutrophils 87.8 high, lymphocytes 2.5 low, lactic acid level 1.4, B type Natriuretic peptide 146.8 high, C reactive protein (CRP) 12.9 high (units and reference range not provided). Serum electrolytes and renal function test results were within normal limits except for chloride 116 high, BUN 29 high, Albumin 2.4 low, globulin 4.0 high, alkaline phosphatase 234 high, magnesium 3.2 high (units and reference range not provided). Arterial blood gases showed pH 7.46 high, pCO2 44, pO2 69 low, base excess 6.5 high, bicarbonate 29.8 high, oxygen saturation of 93%. The family was notified that the subject's condition was critical; his status was Do Not Resuscitate. On 16 Feb 2016, the subject died. An autopsy was not performed. The cause of death was high-grade partial small bowel obstruction . The outcome of the medically significant and life-threatening events was death. The investigator confirmed that he had symptoms of shortness of breath and hypoxia likely due to sepsis. There was no further respiratory testing done, no ICU admission, no additional vital signs available, no documented intubation, and no additional oxygen supplementation other than the previously reported Vapotherm method.

The Principal Investigator assessed the events of small intestinal obstruction, sepsis POA, diverticulitis and pneumonia severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the event of small intestinal obstruction was potentially related to adhesions and the events of sepsis POA, diverticulitis and pneumonia were potentially related to small intestinal obstruction. The Sponsor assessed the events of small intestinal obstruction, sepsis POA, diverticulitis and pneumonia as not related to 2019-20 Fluzone Quadrivalent.

It is important to note the subject had a past medical history significant for hypertension, benign prostatic hyperplasia with obstructive urinary tract, drug allergy to Benzoin, drug allergy to Benzol peroxide, drug allergy to clindamycin, atrial fibrillation, and open sigmoid colectomy with colostomy with reversal (1992). Concomitant medications included Toprol XL, Cardizem CD, tamsulosin, and Coumadin.

Subject number:	US013-1018
Subject demographics:	80-89-year-old White PPD female from the PPD
Vaccine group:	2019-20 Fluzone Quadrivalent
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Feb 2015
Serious adverse event (SAE):	Subarachnoid haemorrhage
Death:	Diffuse subarachnoid hemorrhage
Relationship of SAE/Death to study vaccine:	Not related

Subject US013-1018 was an 80-89-year-old White PPD female from the PPD. She experienced an SAE of subarachnoid hemorrhage on 30 Jun 2015 and died due to the SAE on 11 Jul 2015 after receiving her single dose of 2019-20 Fluzone Quadrivalent.

On 30 Jun 2015, 4 months after administration of 2019-20 Fluzone Quadrivalent, the subject was found outside her front steps. It was presumed that she had fallen 4 to 5 steps and had a loss of consciousness for an unknown length of time. She was transferred to the ER. Upon arrival, she was confused and did not know where she was but was able to follow commands. Examination revealed the subject to be disoriented to time and place with a Glasgow Coma Scale (GCS) total score of 14; her pupils were equal, round, and reacted to light. She denied any visual changes, headache or specific pain. She had a 6 cm scalp laceration and ecchymosis of her PPD A CT of the head and brain without contrast revealed diffuse acute subarachnoid hemorrhage bilaterally, small bilateral subdural hematomas (left greater than right), and hemorrhagic contusions likely involving the left frontal and right temporal lobes. No depressed skull fracture was identified. There was no evidence of an acute infarct. CT of the cervical spine without contrast revealed no acute cervical spine fractures or dislocations. An x-ray of the pelvis showed no dislocations or fractures of the hips, with severe chronic and degenerative changes of the lower spine. A chest x-ray revealed clear lungs, unremarkable heart, hilar and mediastinal shadows, and no acute fracture. Laboratory testing revealed the subject was anemic and hyperkalemic; hemoglobin was 11.4 (low) and hematocrit was 34.8 (low) and potassium was 5.4 (high) (reference ranges and units not provided). Other abnormal laboratory values included a WBC of 11.0 (high), glucose of 117 (high), INR of 0.94, APTT of 34, and prothrombin of 11.0 (reference ranges and units not provided).The subject was intubated and a feeding tube was placed. Her scalp laceration was repaired with staples while in the ER. She was admitted to the intensive care unit. Treatment also included hydralazine as necessary, pain control, and Protonix. On 01 Jul 2015, a repeat CT of the head revealed a significant increase in the size of the contusion in the left frontal lobe. On an unspecified date, the subject had an intracerebral hemorrhage (ICH) score of 5 and a GCS of 4. The subject's family made the decision to place the subject on palliative care. On 06 Jul 2015, she was discharged to the inpatient hospice unit. On 11 Jul 2015, the subject died. The cause of death was diffuse subarachnoid hemorrhage. An autopsy was not performed.

The Principal Investigator assessed the event of subarachnoid hemorrhage as severe and not related to 2019-20 Fluzone Quadrivalent. In the opinion of the Principal Investigator, the event of subarachnoid hemorrhage was potentially related to a fall. The Sponsor assessed the event of subarachnoid hemorrhage as not related to 2019-20 Fluzone Quadrivalent.

It is important to note that the subject had a past medical history significant for type 2 diabetes mellitus, pure hypercholesterolemia, essential hypertension, renal diabetes, aortic incompetence, , diabetic neuropathy, hypothyroidism, ulcerative colitis, , and gastroesophageal reflux disease. Concomitant medications included fluticasone, clonidine, Lovaza, nitroglycerin, rosuvastatin, Proventil HFA, Lasix, amlodipine, hydrochlorothiazide, aspirin, pantoprazole, folic acid, Glucophage, levothyroxine, Levemir FlexTouch U-100, Pentasa, metoprolol, and Benicar.

9.2 Treatment-Related Serious Adverse Events

Two SAEs, 1 case of pericarditis in a participant that received 2 doses of 6.5 µg EBOV GP without adjuvant and 1 case of convulsion in a participant that received 2 doses of 13 µg EBOV GP without adjuvant, were deemed as possibly related to the vaccine by the investigator. However, upon careful review of the participants' medical histories, the sponsor deemed the SAEs as not related to trial vaccine.

Subject number:	US045-1151
Subject demographics:	30-39-year-old Other male from PPD
Vaccine group:	EBOV GP 6.5µg and 0µg Matrix-M1 adjuvant
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	04 Mar 2015
Serious adverse event (SAE):	Pericarditis
Relationship of SAE to study vaccine:	Possibly related

Subject US045-1151 was a 30-39-year-old Other male from PPD . He experienced an SAE of pericarditis on 04 Sep 2015 after receiving his 2 doses of EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant.

The subject received his first intramuscular dose of EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant on 11 Feb 2015 and his second intramuscular dose of EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant on 04 Mar 2015. On 04 Sep 2015, the subject developed sudden onset of chest pain and was seen at the hospital's ED. The event was initially triaged as cardiac chest pain, and the subject underwent a coronary angiogram that showed normal coronary arteries and normal left ventricular systolic function. An ECG showed ST elevation inferior leads. Laboratory results were within normal limits with the exception of creatine phosphokinase (CPK) at 502 U/L (reference range 0-240). The subject was subsequently diagnosed with pericarditis. On an unspecified date, he was discharged home with a 3-month supply of colchicine and ibuprofen 400 mg. On 08 Nov 2015, a transthoracic echocardiography showed normal left ventricle size, normal systolic function, and no significant valve abnormalities. On 25 Dec 2015, the event was considered resolved. On 11 Jan 2016, it was concluded that the subject was in normal sinus rhythm throughout, with rare atrial and ventricular ectopic beats and no significant pauses or sustained arrhythmias upon review of his Holter monitor.

The Principal Investigator assessed the event of pericarditis as moderate and initially assessed the event as not related to EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant but subsequently assessed the event as possibly related to EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant. In the opinion of the Principal Investigator, the event was suspected viral pericarditis though possibly related to trial vaccine given the possible long-term immune-related sequela like Guillain-Barre syndrome with flu vaccination. The Investigator was concerned with a delayed immune-related event. The Sponsor initially assessed the event as unrelated to EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant. The Sponsor subsequently assessed the event as unrelated/unlikely related to EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant, disagreeing with the investigator's upgraded assessment of EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant relationship. The basis of this assessment was the lack of a reasonable temporal relationship of the current event to the EBOV GP 6.5 µg and 0 µg Matrix-M1 adjuvant.

It is important to note that his past medical history was significant for palpitations. No concomitant medications were reported.

Subject number:	US050-1073
Subject demographics:	30-39-year-old White PPD male from PPD
Vaccine group:	EBOV GP 13µg and Matrix-M1 adjuvant 0 µg
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	04 Mar 2015
Serious adverse event (SAE):	Convulsion
Relationship of SAE to study vaccine:	Possibly related

Subject US050-1073 was a 30-39-year-old White PPD male from PPD. He experienced an SAE of convulsion on 22 Dec 2015 after receiving his 2 doses of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant.

The subject received his first intramuscular dose of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant on 11 Feb 2015 and his second intramuscular dose of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant on 04 Mar 2015.

On 12 Aug 2015, during the course of this study, the subject experienced a seizure. On 01 Nov 2015, the subject had an outpatient electroencephalogram (EEG), which was assessed as normal. On 22 Dec 2015, the subject had a seizure after making a plane journey on the same day. The subject experienced a 3- to 4-minute tonic-clonic seizure with no prodrome or preceding illness. He was unconscious for approximately 5 minutes with 5 to 10 minutes of post-ictal confusion. He was taken to a hospital for further evaluation. Laboratory test results were reported within normal limits with the exception of a hemoglobin of 95 g/L (reference range 135-180), hematocrit 0.31 (reference range 0.39-0.53), and red cell count 3.69 × 1012/L (reference range 4.50-6.00). The subject reported PPD prior to the seizure. He reported his PPD during the previous week and his PPD prior to the seizure. On 22 Dec 2015, the event was considered resolved. On 23 Dec 2015, the subject commenced treatment with sodium valproate.

The Principal Investigator assessed the event of convulsion as moderate and possibly related to of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant. In the opinion of the Principal Investigator, the event was most likely related to PPD but it could still be possibly related to of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant given the increase in seizure frequency since commencement of the study (and no seizure activity from the age of PPD), as well as the unexplained decrease in hemoglobin (ie, a possible relationship cannot be ruled out). The Sponsor assessed the event as not related to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant. The basis of this assessment are a) the remoteness of the current event from last test article administration, b) the existence of a well-documented closely similar neurological event in the past medical history which long antedates exposure to the test article, and c) the apparently chronic history of PPD which has been cited as a potential trigger in each recurrence of seizure (including the event which antedates exposure).

It is important to note that the subject had a past medical history significant for a previous seizure at PPD which was triggered by excessive PPD . No concomitant medications were reported.

9.3 Important Adverse Events of Special Interest

There were 4 SAEs (all seizure) reported as PIMMCs, with 2 events each occurring in each age strata.

Subject number:	US025-1161
Subject demographics:	70-79-year-old White PPD male from the PPD
Vaccine group:	Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg (co-form) and Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	11 Mar 2015
Serious adverse event (SAE):	Seizure
Relationship of SAE/death to study vaccine:	Not related

Subject US029-1099 was a 70-79-year-old White PPD male from the PPD . He experienced an SAE of seizure on 04 Aug 2016 after receiving one dose of Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg (co-form) and one dose of placebo. The subject received Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg on 23 Feb 2016 and placebo on 22 Mar 2016.

On 04 Aug 2016, 5 months after administration of Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg (co-form) and 4 months after administration of placebo, the subject experienced a seizure. PPD became alert as EMS was interviewing him. He was taken to the ER and by the time the subject arrived at the hospital, he was completely alert and oriented × 3. An MRI of the head showed mild small vessel ischemic changes, with no evidence of acute intracranial abnormality. A urine culture grew gram negative rods and the subject was treated with Rocephin. He was started on Keppra 500 mg 2 times a day. The subject was in stable condition and he was discharged on a 5-day course of Omnicef. On 17 Aug 2016, the subject had a Neurology consultation during which he denied history of meningitis, encephalitis, any previous neurological condition, history of seizure, or major head trauma with loss of consciousness. The subject reported daytime fatigue and tiredness, and no recurrence of a seizure.

The Principal Investigator assessed the event of seizure as severe and not related to Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg (co-form) and placebo. In the opinion of the Principal Investigator, the event of seizure was potentially related to an unknown etiology. The Sponsor assessed the event of seizure as not related to Quad-NIV 300 µg + Matrix-M1 adjuvant 50 µg (co-form) and placebo.

It is important to note that the subject's past medical history was significant for restless leg syndrome, hypertension, prostatectomy, and bladder cancer. Per the medical records, the subject's medical history also included hypercholesterolemia. Concomitant medications included Carbidopa/Levodopa, Ropinirole, Trazodone, and vitamin C.

Subject number:	US029-1017
Subject demographics:	70-79-year-old White PPD female from the PPD
Vaccine group:	Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg (co-form) and Placebo
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	10 Mar 2015
Serious adverse event (SAE):	Seizure
Relationship of SAE/death to study vaccine:	Not related

Subject US029-1017 was a 70-79-year-old White PPD female from the PPD. She experienced seizure on 23 Jul 2015 after receiving one dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg (co-form) and one dose of placebo. The subject received Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg on 11 Feb 2015 and placebo on 10 Mar 2015.

On 22 Jul 2015, the subject experienced PPD numbness or tingling, difficulty speaking and inability to swallow correctly. Following the onset of those symptoms, the subject believed she experienced several episodes of seizure-like activity while lying on a couch.

On 23 Jul 2015, 5 months after administration of the first dose of Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg and 4 months after administration of placebo, the subject experienced a worsening of seizure disorder. As her symptoms resolved, she presented to the ER to be evaluated. In the ER, the subject denied any seizure- like activity and specific numbness or tingling to her face, arms or legs. A physical examination was unremarkable. The subject had no lateralizing neurologic focal deficits. The National Institutes of Health (NIH) stroke score was 0. The subject's complete blood count (CBC), and comprehensive metabolic panel (CMP) were unremarkable. She was admitted to the hospital with possible transient ischemic attack (TIA) versus seizures. On admission, the subject's phenytoin level was sub-therapeutic at 7.4. She was given a loading dose of fosphenytoin 500 mg IV. A CT of the head showed remote lacunar infarcts of the brainstem and basal ganglia, and chronic ischemia attributed to degenerative microangiopathy in the periventricular/subcortical region. There were no acute findings, excluding a new cerebral vascular accident (CVA). An echocardiogram showed normal left ventricular size and systolic function, ejection fraction 65%, grade 1 diastolic dysfunction and no significant valvular abnormalities. A bilateral carotid Doppler suggested 50% to 70% stenosis in the proximal left internal carotid. A CTA of the neck showed normal carotid arteries with no significant stenosis. MRI of the brain showed chronic ischemia with remote lacunar infarcts. The subject was started on baby aspirin once a day and her phenytoin dose was increased to 150 mg twice a day. The subject had no further evidence of seizure activity. On 25 Jul 2015, the subject was discharged home in stable condition without further seizure activity while hospitalized. The event was considered resolved.

The Principal Investigator assessed the event of seizure as severe and not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg (co-form) and placebo. In the opinion of the Principal Investigator, the event of seizure was potentially related to underlying medical condition (seizure disorder). The Sponsor assessed the event of seizure as not related to Quad-NIV 240 µg + Matrix-M1 adjuvant 50 µg (co-form) and one dose of placebo.

It is important to note that the subject's past medical history was significant for seizure disorder, and cerebral vascular accident. Concomitant medications included phenytoin.

Subject number:	US050-1105
Subject demographics:	30-39-year-old White male from the PPD
Vaccine group:	EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	04 Mar 2015
Serious adverse event (SAE):	Seizure
Relationship of SAE/death to study vaccine:	Not related

Subject US050-1105 is a 30-39-year-old White male from PPD. experienced seizure on 09 Aug 2015 after receiving two doses EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant.

On 12 Aug 2015, 6 months after the initial dose of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant and 5 months after the second dose of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant, the subject experienced seizure while sitting in a chair at his workplace having a drink and smoke after work and fell. The subject recalled nothing until he woke up in the ambulance feeling very tired. There were no triggers identified as the subject had been well for the previous week. There was no change in medications and no new drug use. The subject reported a headache, which lasted all day long on the day of the seizure. The subject reported daily PPD but was unsure if he had used more than usual on the day of the seizure. The subject was admitted to hospital and upon examination, two small ecchymoses on the back of the head were noted, but no hematoma was palpable. His neurological observations (tone, power, reflexes, coordination, and sensation in upper and lower limbs) and his cranial nerves were normal. His vital signs were stable. An ECG was normal. The subject was monitored in the ED short stay unit overnight. On 13 Aug 2015, a CT of the brain (non-contrast) was performed which showed no acute intracranial abnormalities. No EEG was performed. The subject was discharged and the event of seizure was considered resolved.

The Principal Investigator assessed the event of seizure as severe and not related to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant. In the opinion of the Principal Investigator, the event was related to possible substance use. The Sponsor assessed the event as unrelated to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant.

It is important to note that the subject's past medical history was significant for a previous seizure at PPD which was triggered by excessive PPD. The subject was not taking any concomitant medications but has used PPD intermittently since 1999.

Subject number:	US050-1105
Subject demographics:	30-39-year-old White male from PPD
Vaccine group:	EBOV GP 13µg and 0µg Matrix-M1 adjuvant
Date of first dose of study vaccine:	11 Feb 2015
Date of last dose of study vaccine:	04 Mar 2015
Serious adverse event (SAE):	Seizure
Relationship of SAE/death to study vaccine:	Possibly related

Subject US050-1105 is a 30-39-year-old White male from PPD. experienced seizure on 22 Dec 2015 after receiving two doses EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant.

On 22 Dec 2015, 10 months after the initial dose of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant and 9 months after the second dose of EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant, the subject experienced a seizure after making a plane journey. The subject experienced a 3-to-4-minute tonic-clonic seizure outside the home of a family member. No prodrome or preceding illness was noted. The subject was unconscious for approximately five minutes with five to ten minutes of post-ictal confusion. He was taken to a hospital for further evaluation. Laboratory results were within normal limits with the exception of hemoglobin 95 g/L (reference range 135-180), hematocrit 0.31 (reference range 0.39-0.52) and red cell count 3.69 × 10^{12}/L (reference range 4.50-6.00). No additional diagnostic testing was performed. The subject reported PPD prior to the seizure. The subject reported his PPD during the previous week and his PPD prior to the seizure. On 23 Dec 2015, the subject commenced treatment with sodium valproate (dose and details of administration not known) which was ongoing at the time of this report.

The Principal Investigator assessed the event of seizure as moderate and possibly related to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant. In the opinion of the Principal Investigator, the event was most likely related to PPD, but it could still be possibly related to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant given the increase in seizure frequency since commencement of the study (and no seizure activity from the age of PPD) as well as the unexplained decrease in hemoglobin (ie, a possible relationship cannot be ruled out). The Sponsor assessed the event as not related to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant due to the remoteness of the current event from last test article administration, the existence of a well-documented closely similar neurological event in the past medical history which long antedated exposure to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant, and the apparently chronic history of PPD, which had been cited as a potential trigger in each recurrence of seizure (including the event which antedated exposure).

It is important to note that the subject's medical history was significant for a previous seizure at PPD, which was triggered by excessive PPD. During the course of the study, the subject also experienced a seizure on 12 Aug 2015, which was assessed by the site investigator as not related to EBOV GP 13 µg and 0 µg Matrix-M1 adjuvant. Thus, the prior episode of Seizure on 12 Aug 2015 was deemed by the site investigator to be likely due to PPD. The subject had attended a neurological outpatient clinic for an EEG on 01 Nov 2015. The EEG was assessed as normal. As part of this event, the subject indicated to hospital staff that he had never been treated for epilepsy. No concomitant medications were reported.