Electronic Supplementary Material

Manuscript Title: Brand-specific enhanced safety surveillance study of GSK's quadrivalent seasonal influenza vaccine, conducted during the COVID-19 pandemic, in Belgium, Germany and Spain, for the 2020/21 season.

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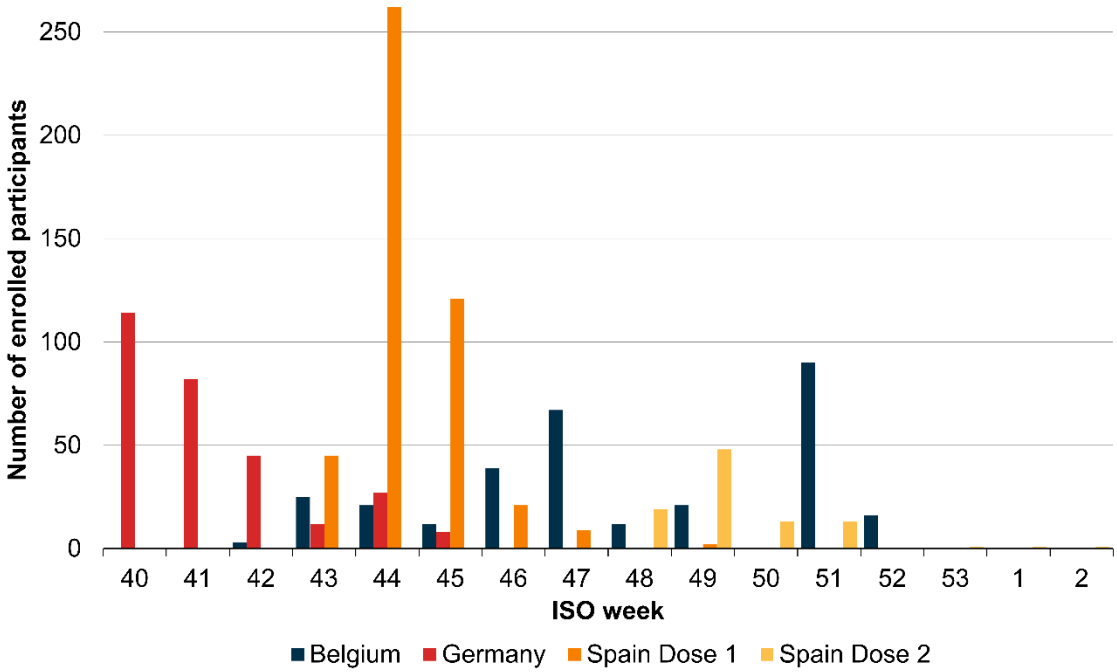
Fig. S1 Number of enrolled participants by ISO week, post-Dose 1 or post-Dose 2, and by country (Safety set)



ISO: International Organization for Standardization

Participants were enrolled from ISO week 40, 2020 (28 September – 4 October 2020) to ISO week 2, 2021 (11 – 17 January 2021)

Table S1. Vaccines co-administered with GSK's IIV4 (Safety set)

GSK IIV4	Co-administered vaccine class[a]	Belgium N=306		Germany N=288		Spain N=460		Total N=1054	
		n	%	n	%	n	%	n	%
Dose 1	**Any**	**4**	**1.3**	**4**	**1.4**	**83**	**18.0**	**91**	**8.6**
	Bacterial + Viral	0	0.0	0	0.0	7	1.5	7	0.7
	Bacterial	0	0.0	0	0.0	1	0.2	1	0.1
	Encephalitis	0	0.0	4	1.4	0	0.0	4	0.4
	Hib	0	0.0	0	0.0	1	0.2	1	0.1
	Hepatitis	0	0.0	0	0.0	49	10.7	49	4.6
	Meningococcal	0	0.0	0	0.0	4	0.9	4	0.4
	Multiple	0	0.0	0	0.0	2	0.4	2	0.2
	Other Bacterial	0	0.0	0	0.0	20	4.3	20	1.9
	Other Viral	0	0.0	0	0.0	6	1.3	6	0.6
	Papillomavirus	0	0.0	0	0.0	2	0.4	2	0.2
	Pertussis	0	0.0	0	0.0	2	0.4	2	0.2
	Pneumococcal	4	1.3	0	0.0	32	7.0	36	3.4
	Poliomyelitis	0	0.0	0	0.0	1	0.2	1	0.1
	Varicella Zoster	0	0.0	0	0.0	3	0.7	3	0.3
	Viral	0	0.0	0	0.0	1	0.2	1	0.1
						Spain N=96		**Total N=96**	
Dose 2	**Any**					**0**	**0.0**	**0**	**0.0**

[a]Vaccination classes coded using GSK's Drug Dictionary

Hib: *Haemophilus influenzae* B; IIV4: inactivated quadrivalent seasonal influenza vaccine; N: number of participants vaccinated with GSK's IIV4; n/%: number/percentage of participants who received the specified co-administered vaccine on the same day as GSK's IIV4

Table S2. COVID-19 suspected, probable and confirmed infections (Safety set)

COVID-19 test	COVID-19 infection[a]	Belgium N=306	Germany N=288	Spain N=460	Total N=1054
		n (%)	n (%)	n (%)	n (%)
During the study[b]	Confirmed	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)
	Probable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Suspected	2 (0.7)	0 (0.0)	1 (0.2)	3 (0.3)
Before the study[c]	Confirmed	1 (0.3)	0 (0.0)	1 (0.2)	2 (0.2)
	Probable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Suspected	11 (3.6)	0 (0.0)	0 (0.0)	11 (1.0)
Total (among tested)	**Any COVID-19 infection**	**14 (4.6)**	**0 (0.0)**	**3 (0.7)**	**17 (1.6)**
Not tested	Confirmed	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)
	Probable	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)
	Suspected	2 (0.7)	0 (0.0)	1 (0.2)	3 (0.3)
Total (among not tested)	**Any COVID-19 infection**	**3 (1.0)**	**0 (0.0)**	**2 (0.4)**	**5 (0.5)**

[a]COVID-19 case definition is based on World health organization case definitions as of 20 March 2020; [b]COVID-19 test performed after informed consent date; [c]COVID-19 test performed before informed consent date

COVID-19: coronavirus disease 2019; N: number of participants; n (%): number (percentage) of participants in a given category

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Table S3. Cumulative participants (%) reporting AEs post-Dose 2 by week (Safety set)

ISO weeks	Spain N=460		
	N	n (%)	95% CI, LL-UL
40-48	19	1 (5.3)	0.1-26.0
40-49	67	9 (13.4)	6.3-24.0
40-50	80	11 (13.8)	7.1-23.3
40-51	93	13 (14.0)	7.7-22.7
40-52	93	13 (14.0)	7.7-22.7
40-53	94	13 (13.8)	7.6-22.5
40-01[a]	95	13 (13.7)	7.5-22.3
40-02[a]	96	13 (13.5)	7.4-22.0

[a]ISO week of 2021

AE: adverse event; ISO: International Organization for Standardization; N: number of participants vaccinated with GSK's inactivated quadrivalent seasonal influenza vaccine (IIV4) in the specified ISO weeks who received an adverse drug reaction (ADR) card; n (%): number (percentage) of participants vaccinated with GSK's IIV4 in the specified ISO week reporting at least one symptom on their ADR card; 95% CI, LL-UL: 95% confidence interval (Clopper-Pearson exact CI not extended for clustered data), lower limit-upper limit

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Table S4. Cumulative participants (%) reporting AEs by severity after each dose (all countries) or both doses (Spain) (Safety set)

Severity grade[a]	Belgium N=306		Germany N=288		Spain N=460		Total N=1054	
	n* AEs	n (%) 95% CI, LL-UL	n* AEs	n (%) 95% CI, LL-UL	n* AEs	n (%) 95% CI, LL-UL	n* AEs	n (%) 95% CI, LL-UL
Post-Dose 1								
Any AE	**214**	**113 (36.9) 8.8-74.1**	**315**	**97 (33.7) 6.6-72.8**	**418**	**188 (40.9) 0.0-99.9**	**947**	**398 (37.8) 29.0-47.2**
Mild	172	81 (26.5) 2.4-71.8	202	52 (18.1) 5.4-39.2	236	107 (23.3) 0.7-76.8	610	240 (22.8) 17.2-29.2
Moderate	41	31 (10.1) 7.0-14.1	100	40 (13.9) 1.9-40.8	134	55 (12.0) 0.0-63.6	275	126 (12.0) 9.0-15.5
Severe	1	1 (0.3) 0.0-10.4	13	5 (1.7) 0.1-8.7	39	23 (5.0) 0.0-97.5	53	29 (2.8) 0.6-7.6
Missing	0	0 (0.0) 0.0-1.2	0	0 (0.0) 0.0-1.3	9	3 (0.7) 0.0-35.9	9	3 (0.3) 0.0-1.5
Post-Dose 2: Spain N=96								
Any AE	**-**	**-**	**-**	**-**	**19**	**13 (13.5) 7.4-22.0**		
Mild	-	-	-	-	11	8 (8.3) 3.7-15.8		
Moderate	-	-	-	-	6	3 (3.1) 0.7-8.9		
Severe	-	-	-	-	2	2 (2.1) 0.3-7.3		
Post-Doses 1 and 2: Spain N=460								
Any AE	**-**	**-**	**-**	**-**	**437**	**193 (42.0) 0.0-99.8**		
Mild	-	-	-	-	247	110 (23.9) 1.7-69.9		
Moderate	-	-	-	-	140	56 (12.2) 0.1-59.6		
Severe	-	-	-	-	41	25 (5.4) 0.0-94.3		
Missing	-	-	-	-	9	2 (0.4)[b] 0.0-25.6		

None of the events reported were classified as potentially life-threatening[a]

[a]**Mild**: symptoms causing no or minimal interference with usual social and functional activities with intervention not indicated; **Moderate**: symptoms causing greater than minimal interference with usual social and functional activities with intervention indicated; **Severe**: symptoms causing inability to perform usual social and functional activities with intervention or hospitalization indicated; **Potentially life-threatening**: symptoms causing inability to perform basic self-care functions with intervention indicated to prevent permanent impairment, persistent disability, or death

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[b]Of the three participants with missing severity data post-Dose 1 in Spain, one participant was classified as "moderate" severity post-Dose 2; therefore, only two participants remain with missing data post-Doses 1 and 2

AE: adverse event; N: number of participants vaccinated with GSK's inactivated quadrivalent seasonal influenza vaccine (IIV4) who received an adverse drug reaction (ADR) card; n[*]: number of AEs reported by severity grade; n (%): number (percentage) of participants vaccinated with GSK's IIV4 per severity grade, considering the more severe report in case of multiple reports; 95% CI, LL-UL: 95% confidence interval (extended Clopper-Pearson exact CI for clustered data) lower limit-upper limit

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Table S5. Cumulative participants (%) reporting AEIs (in italics) and/or other AEs post-Doses 1 and 2 classified by MedDRA Primary System Organ Class over the study period - Spain (Safety set)

MedDRA Primary System Organ Class (Code) Preferred Term (Code)	Spain N=460		
	n[a]	n	% [95% CI, LL-UL]
Any	**437**	**193**	**42.0 [0.0-99.8]**
General disorders and administration site conditions (10018065)	**271**	**166**	**36.1 [0.0-99.9]**
Injection site pain (10022086)	*149*	*144*	*31.3 [0.0-99.8]*
Injection site swelling (10053425)	*40*	*40*	*8.7 [0.0-98.3]*
Fatigue (10016256)	*30*	*29*	*6.3 [0.0-98.0]*
Injection site erythema (10022061)	*24*	*24*	*5.2 [0.0-51.2]*
Pyrexia (10037660)	*15*	*15*	*3.3 [0.1-16.3]*
Chills (10008531)	*13*	*13*	*2.8 [0.0-91.8]*
Nervous system disorders (10029205)	**40**	**36**	**7.8 [0.0-100.0]**
Headache (10019211)	*34*	*34*	*7.4 [0.0-100.0]*
Dizziness (10013573)	*5*	*5*	*1.1 [0.0-78.8]*
Clumsiness (10009696)	1	1	0.2 [0.0-45.9]
Gastrointestinal disorders (10017947)	**36**	**25**	**5.4 [0.0-49.9]**
Diarrhoea (10012735)	*14*	*13*	*2.8 [0.0-45.0]*
Vomiting (10047700)	*11*	*11*	*2.4 [0.0-30.7]*
Nausea (10028813)	*11*	*11*	*2.4 [0.0-26.0]*
Musculoskeletal and connective tissue disorders (10028395)	**33**	**24**	**5.2 [0.0-100.0]**
Myalgia (10028411)	*21*	*21*	*4.6 [0.0-99.7]*
Arthralgia (10003239)	*9*	*9*	*2.0 [0.0-92.4]*
Pain in extremity (10033425)	2	2	0.4 [0.0-8.6]
Limb discomfort (10061224)	1	1	0.2 [0.0-45.9]
Respiratory, thoracic and mediastinal disorders (10038738)	**24**	**16**	**3.5 [2.0-5.6]**
Rhinorrhoea (10039101)	*12*	*12*	*2.6 [0.0-17.2]*
Cough (10011224)	5	5	1.1 [0.0-12.2]

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Nasal congestion (10028735)	4	4	0.9 [0.0-4.7]
Sneezing (10041232)	2	2	0.4 [0.0-25.6]
Pharyngeal swelling (10082270)	1	1	0.2 [0.0-45.9]
Metabolism and nutrition disorders (10027433)	**13**	**13**	**2.8 [1.5-4.8]**
Decreased appetite (10061428)	*13*	*13*	*2.8 [1.5-4.8]*
Skin and subcutaneous tissue disorders (10040785)	**10**	**9**	**2.0 [0.0-15.9]**
Pruritus (10037087)	*7*	*7*	*1.5 [0.4-4.0]*
Rash (10037844)	*2*	*2*	*0.4 [0.0-25.6]*
Eczema (10014184)	1	1	0.2 [0.0-13.7]
Psychiatric disorders (10037175)	**7**	**7**	**1.5 [0.0-29.8]**
Irritability (10022998)	*7*	*7*	*1.5 [0.0-29.8]*
Infections and infestations (10021881)	**2**	**2**	**0.4 [0.0-8.6]**
Nasopharyngitis (10028810)	1	1	0.2 [0.0-45.9]
Suspected COVID-19 (10084451)	1	1	0.2 [0.0-13.7]
Eye disorders (10015919)	**1**	**1**	**0.2 [0.0-45.9]**
Eye allergy (10015907)	*1*	*1*	*0.2 [0.0-45.9]*

In italics: predefined adverse events of interest (AEIs) listed on the adverse drug reaction (ADR) card

AE: adverse event; Any: at least one symptom experienced (regardless of the MedDRA preferred term) under the specified system organ class; COVID-19: coronavirus disease 2019; MedDRA: Medical Dictionary for Regulatory Activities; N: total number of participants vaccinated with at least one dose of GSK's inactivated quadrivalent seasonal influenza vaccine (IIV4) and who received the corresponding ADR card; n[a]: number of specified AEs reported considering both ADR cards; n/%: number/percentage of participants vaccinated with at least one dose of GSK's IIV4 reporting the symptom at least once considering both ADR cards; 95% CI, LL-UL: 95% confidence interval (extended Clopper-Pearson exact CI for clustered data), lower limit-upper limit

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Table S6. Cumulative participants (%) with or without co-administered vaccination, reporting AEIs (italics) and/or other AEs post-Dose 1 classified by MedDRA Primary System Organ Class over the study period (Spain, Safety set)

MedDRA Primary System Organ Class (Code) **Preferred Term (Code)**	**Co-administration** **N=83** **n (%)** **95% CI, LL-UL**	**No co-administration** **N=377** **n (%)** **95% CI, LL-UL**
Any	**42 (50.6)** **39.4-61.8**	**146 (38.7)** **0.1-99.2**
General disorders and administration site conditions (10018065)	**37 (44.6)** **33.7-55.9**	**124 (32.9)** **0.0-99.8**
Injection site pain (10022086)	*29 (34.9)* *24.8-46.2*	*113 (30.0)* *0.0-99.9*
Injection site swelling (10053425)	*14 (16.9)* *9.5-26.7*	*23 (6.1)* *0.0-86.8*
Fatigue (10016256)	*9 (10.8)* *5.1-19.6*	*19 (5.0)* *0.0-95.3*
Injection site erythema (10022061)	*9 (10.8)* *5.1-19.6*	*15 (4.0)* *0.8-11.3*
Chills (10008531)	*9 (10.8)* *5.1-19.6*	*4 (1.1)* *0.0-20.6*
Pyrexia (10037660)	*3 (3.6)* *0.8-10.2*	*12 (3.2)* *0.1-15.4*
Gastrointestinal disorders (10017947)	**5 (6.0)** **2.0-13.5**	**19 (5.0)** **0.0-68.9**
Nausea (10028813)	*5 (6.0)* *2.0-13.5*	*6 (1.6)* *0.0-29.5*
Diarrhoea (10012735)	*2 (2.4)* *0.3-8.4*	*11 (2.9)* *0.0-48.0*
Vomiting (10047700)	*2 (2.4)* *0.3-8.4*	*8 (2.1)* *0.0-37.5*
Nervous system disorders (10029205)	**19 (22.9)** **14.4-33.4**	**17 (4.5)** **0.0-93.0**
Headache (10019211)	*19 (22.9)* *14.4-33.4*	*15 (4.0)* *0.0-74.7*
Dizziness (10013573); Clumsiness (10009696)	*2;* 0 NR	*3;* 1 NR
Musculoskeletal and connective tissue disorders (10028395)	**10 (12.1)** **5.9-21.0**	**14 (3.7)** **0.0-99.5**
Myalgia (10028411)	*9 (10.8)* *5.1-19.6*	*12 (3.2)* *0.0-96.9*
Arthralgia (10003239)	*4 (4.8)* *1.3-11.9*	*5 (1.3)* *0.0-78.0*
Pain in extremity (10033425); Limb discomfort (10061224)	0; 0 NR	2; 1 NR
Respiratory, thoracic and mediastinal disorders (10038738)	**2 (2.4)** **0.3-8.4**	**12 (3.2)** **0.1-15.4**
Rhinorrhoea (10039101)	*2 (2.4)* *0.3-8.4*	*8 (2.1)* *0.0-43.4*
Cough (10011224)	1 (1.2) 0.0-6.5	4 (1.1) 0.0-20.6
Nasal congestion (10028735); Sneezing (10041232); Pharyngeal swelling (10082270)	1; 0; 1 NR	3; 2; 0 NR
Metabolism and nutrition disorders (10027433)	**4 (4.8)** **1.3-11.9**	**8 (2.1)** **0.0-37.5**

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Decreased appetite (10061428)	*4 (4.8)* *1.3-11.9*	*8 (2.1)* *0.0-37.5*
Skin and subcutaneous tissue disorders (10040785)	**2 (2.4)** **0.3-8.4**	**6 (1.6)** **0.0-29.5**
Pruritus (10037087)	*2 (2.4)* *0.3-8.4*	*4 (1.1)* *0.0-20.6*
Rash (10037844); Eczema (10014184)	*0;* 0 NR	*2;* 1 NR
Psychiatric disorders (10037175)	**1 (1.2)** **0.0-6.5**	**5 (1.3)** **0.0-25.2**
Irritability (10022998)	*1 (1.2)* *0.0-6.5*	*5 (1.3)* *0.0-25.2*
Infections and infestations (10021881)	**1 (1.2)** **0.0-6.5**	**1 (0.3)** **0.0-5.6**
Suspected COVID-19 (10084451); Nasopharyngitis (10028810)	0; 1 NR	1; 0 NR
Eye disorders (10015919)	**0 (0.0)** **0.0-4.4**	**1 (0.3)** **0.0-67.1**
Eye allergy (10015907)	*0 (0.0)* *0.0-4.4*	*1 (0.3)* *0.0-67.1*

In italics: predefined adverse events of interest (AEIs) listed on the adverse drug reaction (ADR) card

AE: adverse event; Any: at least one symptom experienced (regardless of the MedDRA preferred term) under the specified system organ class; COVID-19: coronavirus disease 2019; MedDRA: Medical Dictionary for Regulatory Activities; N: total number of participants vaccinated with GSK's inactivated quadrivalent seasonal influenza vaccine (IIV4) who received an ADR card; n (%): number (percentage) of participants vaccinated with GSK's IIV4 reporting the symptom at least once on their ADR card; NR: AEs that occurred in three or fewer cases were grouped to simplify the table, with the number of cases presented for each symptom and the total number (%) for each symptom, but not each individual 95% CI; 95% CI, LL-UL: 95% confidence interval (extended Clopper-Pearson exact CI for clustered data), lower limit-upper limit

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