HyQvia

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
II/0078	Update of section 4.8 and 5.1 of the SmPC in order to update safety data in paediatric population based on final results from study 161504 – Post-Authorization Safety, Tolerability and Immunogenicity Evaluation of HyQvia in Pediatric Subjects With Primary Immunodeficiency Diseases,	27/10/2022		SmPC, Annex II and PL	

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	listed as a category 3 study in the RMP. This is a paediatric interventional Phase 4 study performed to acquire additional data on safety, tolerability and immunogenicity of HyQvia in paediatric (age two to <18 years) patients with Primary Immunodeficiency Diseases (PIDD). In addition, the MAH is taking this opportunity to update Annex II-D of the PI following procedure EMEA/H/C/002491/II/0070/G, and to remove the statement that this medicinal product is subject to additional monitoring from the SmPC and Package leaflet following the fulfilment of the PASS 161302. The RMP version 13.1 has also been adopted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0084	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	05/10/2022	n/a		
IA/0083	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	23/08/2022	n/a		
IAIN/0081	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) -	13/07/2022	n/a		

	Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
N/0079	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/06/2022		PL	
WS/2240	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	19/05/2022	n/a		
SW/0080	Post Authorisation Safety Study results - EMEA/H/C/PSR/S/0037 – Variation	24/02/2022	29/04/2022	Annex II	The final study report submitted by the MAH complies with their obligation to perform a PASS to evaluate the long-term safety and use of HyQvia in patients receiving treatment with HyQvia as imposed at the time of the initial marketing authorisation.
IA/0076/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the	24/01/2022	n/a		

	finished product, including quality control sites (excluding manufacturer for batch release) A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)				

WS/2060	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	21/10/2021	n/a		
WS/2099	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	14/10/2021	n/a		
II/0070/G	This was an application for a group of variations. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/09/2021	04/02/2022	SmPC and PL	In view of the very limited data from the result of a non-interventional, prospective, uncontrolled, two-arm, open-label, multicentre post-authorisation pregnancy registry of women treated with HyQvia, section 4.6 of the SmPC has been updated to state that from a total of nine women enrolled in this study, and of the eight pregnancies with known outcomes, there were eight live births with normal APGAR scores. There were no specified labor or delivery complications. Four mothers were tested for anti rHuPH20 binding or neutralizing antibodies and no antibodies were detected. Subsection Breast-feeding of section 4.6 has been updated to add that one infant in the study was breastfed and that all adverse events were reported as not related to previous or current HyQvia treatment.

					Section B point 2 of the Package Leaflet is updated accordingly and several editorial changes that do not change the content of the previously approved SmPC are introduced in sections 3, 4.2, 4.4 and 4.7. For more information, please refer to the Summary of Product Characteristics.
N/0074	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/08/2021	04/02/2022	PL	
IAIN/0075	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	08/07/2021	n/a		
WS/1964	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product	08/07/2021	n/a		
II/0068/G	This was an application for a group of variations. B.II.c.1.d - Change in the specification parameters and/or limits of an excipient - Change outside the approved specifications limits range B.II.c.1.b - Change in the specification parameters	08/07/2021	n/a		

	and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.II.c.2.b - Change in test procedure for an excipient - Deletion of a test procedure if an alternative test procedure is already authorised B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits				

	B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile) B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line) B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol				

	product and any of the test methods at the site is a biol/immunol method B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test				

	method or a method using a biological reagent B.II.c.1.e - Change in the specification parameters and/or limits of an excipient - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting				

	material [-] used in the manufacture of a biological/immunological product				
WS/2047	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/05/2021	n/a		
WS/1984	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size	11/02/2021	n/a		
IB/0067	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	02/02/2021	04/02/2022	Annex II	
PSUSA/1633/ 202005	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	14/01/2021	n/a		PRAC Recommendation - maintenance
IA/0065/G	This was an application for a group of variations. B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an	08/12/2020	n/a		

	alternative method is already authorised B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised				
WS/1924	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	26/11/2020	n/a		
WS/1882	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	17/09/2020	n/a		

II/0056	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/07/2020	03/09/2020	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'HyQvia-H-C-002491-II-0056'
IAIN/0062	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	20/08/2020	n/a		
IB/0061	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	11/08/2020	n/a		
IAIN/0059/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	20/05/2020	n/a		
N/0057	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/04/2020	03/09/2020	PL	

II/0055	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	17/04/2020	n/a		
II/0054	B.II.e.4.b - Change in shape or dimensions of the container or closure (immediate packaging) - The change in shape or dimensions concerns a fundamental part, which may have a significant impact on the delivery, use, safety or stability of the FP	12/03/2020	n/a		
WS/1524	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.2 - Introduction of a post approval change management protocol related to the AS	20/02/2020	n/a		
IA/0052/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code A.7 - Administrative change - Deletion of manufacturing sites	09/01/2020	03/09/2020	SmPC, Annex II and PL	
II/0051	B.II.c.1.d - Change in the specification parameters and/or limits of an excipient - Change outside the approved specifications limits range	19/09/2019	n/a		

IAIN/0050/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	20/06/2019	n/a		
WS/1519/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product	14/06/2019	n/a		
WS/1500/G	This was an application for a group of variations following a worksharing procedure according to	16/05/2019	n/a		

	Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.V.a.1.b - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - First-time inclusion of a new PMF NOT affecting the properties of the FP A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
IB/0049	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	15/05/2019	n/a		
WS/1494	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	07/03/2019	n/a		

IB/0043	B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	22/10/2018	n/a		
WS/1407	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	13/09/2018	n/a		
II/0040/G	This was an application for a group of variations. Update of section 4.8 of the SmPC to include aseptic meningitis as adverse reaction. The PL is updated accordingly. Update of section 4.2 of the SmPC to include the option of hand-push administration of the rHuPH20 component (in addition to administration with a pump). This change is a correction in order to harmonise with the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/07/2018	19/07/2019	SmPC and PL	The IG 10% component should be infused using a pump. The rHuPH20 may be hand-pushed or infused by a pump. A 24 gauge needle may be required to allow patients to infuse at flow rates of 300 mL/hr/infusion site. However, needles with smaller diameters may be used if slower flow rates are acceptable.
IAIN/0041	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier	23/04/2018	n/a		

	of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
WS/1309	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products	08/02/2018	n/a		
PSUSA/1633/ 201705	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	11/01/2018	n/a		PRAC Recommendation - maintenance
R/0037	Renewal of the marketing authorisation.	09/11/2017	08/01/2018		
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/06/2017	08/01/2018	PL	
IAIN/0035	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	28/04/2017	n/a		
WS/1085	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.III.1.a.2 - Submission of a new/updated or	21/04/2017	n/a		

	deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
II/0033/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent	23/03/2017	n/a		
II/0032	Update of section 4.2 and 4.8 of the SmPC in order to add information on infusion site leakage. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/03/2017	08/01/2018	SmPC, Labelling and PL	Infusion site leakage can occur during or after subcutaneous administration of immunoglobulin, including HyQvia. Consider using longer needles and/or more than one infusion site. Any change of needle size would have to be supervised by the treating physician.
PSUSA/1633/ 201605	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	12/01/2017	n/a		PRAC Recommendation - maintenance

WS/1003	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	15/12/2016	n/a		
WS/0966	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	15/09/2016	n/a		
IAIN/0029	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	11/07/2016	n/a		
WS/0882/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished	09/06/2016	n/a		

	product - Tightening of in-process limits B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
II/0021	Extension of indication to include paediatric population for all authorised indications: as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	28/04/2016	01/06/2016	SmPC and PL	Please refer to the Scientific Discussion HyQvia-H-C-2491-II-021.
IAIN/0027/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	28/04/2016	26/05/2016	Annex II	
II/0022	Update of section 4.4 "Special warnings and precautions for use" of the HyQvia SmPC to add information that aseptic meningitis syndrome (AMS)	25/02/2016	26/05/2016	SmPC, Labelling and PL	

	occurs independently of high or low dosage and that it also occurs more frequently in women than men based on PV data collected on AMS and to provide new information on possible false positive reading of assays used for diagnosis of fungal infections depending on detection of beta-D-glucans. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement the new Guideline on core SmPC for human normal immunoglobulin for subcutaneous and intramuscular administration (EMA/CHMP/BPWP/143744/2011 rev. 1), which came into force on 1 September 2015, as well as the current QRD template version 9.1 with the present submission. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0024	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	02/02/2016	26/05/2016	SmPC	
IA/0026	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	27/01/2016	n/a		
WS/0825	This was an application for a variation following a worksharing procedure according to Article 20 of	14/01/2016	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product				
PSUSA/1633/ 201505	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	14/01/2016	n/a		PRAC Recommendation - maintenance
WS/0790	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier	19/11/2015	26/05/2016	Annex II	
IB/0020	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	20/10/2015	n/a		
IB/0018	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	30/09/2015	n/a		
WS/0720	This was an application for a variation following a worksharing procedure according to Article 20 of	16/07/2015	n/a		

	Commission Regulation (EC) No 1234/2008. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes				
II/0013	Update of sections 4.2, 4.4, 4.6 and 5.3 of the SmPC in order to update the safety information regarding pregnancy, fertility and lactation following new additional preclinical data. The Package Leaflet is updated accordingly. Furthermore, the Annex II has been revised to remove educational material based on the availability of additional new data. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet and to make minor editorial changes to the SmPC and PL (including additional minor modifications to the handling instructions and pictograms in the PL). The updated RMP version 7.0 has been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/06/2015	26/05/2016	SmPC, Annex II and PL	The safety of HyQvia for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women and breast-feeding mothers. SCIg products have been shown to cross the placenta, increasingly during the third trimester. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected. Development and reproductive toxicology studies have been conducted with recombinant human hyaluronidase in mice and rabbits. No adverse effects on pregnancy and foetal development were associated with anti-rHuPH20 antibodies and extensive nonclinical safety data package does not support prior theoretical concerns that anti-rHuPH20 antibodies could potentially affect fertility or pregnancy. In these studies, maternal antibodies to recombinant human hyaluronidase were transferred to offspring in utero. The effects of antibodies to the recombinant human hyaluronidase component of HyQvia on the human embryo or on human foetal development are currently unknown.

					If a woman becomes pregnant, the treating physician should encourage her to participate in the pregnancy registry. Immunoglobulins are excreted into the milk and may contribute to protecting the neonate from pathogens which have a mucosal portal of entry. There are currently no clinical safety data for HyQvia on fertility available. In conclusion, the available data indicates that administration of the rHuPH20 component of HyQvia to pregnant women or individuals of child-bearing potential does not impose an additional safety risk.
IAIN/0016	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	03/06/2015	26/05/2016	Annex II and PL	
IAIN/0015/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient C.I.8.a - Introduction of or changes to a summary of	26/05/2015	26/05/2016	SmPC, Annex II, Labelling and PL	

	Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IB/0012/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation A.7 - Administrative change - Deletion of manufacturing sites	26/03/2015	n/a		
WS/0683	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	26/03/2015	n/a		
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/03/2015	26/05/2016	PL	
WS/0670	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished	26/02/2015	n/a		

	product - Other changes to a test procedure (including replacement or addition)				
PSUSA/1633/ 201405	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	09/01/2015	n/a		PRAC Recommendation - maintenance
WS/0585/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change in test procedure for AS B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	23/10/2014	n/a		
IB/0006/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	08/08/2014	n/a		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
PSUV/0004	Periodic Safety Update	13/06/2014	n/a		PRAC Recommendation - maintenance
IAIN/0005/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	30/04/2014	n/a		
IAIN/0003	C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring	18/12/2013	16/12/2014	SmPC, Labelling and PL	
II/0002/G	This was an application for a group of variations. Change in the manufacturing process of the active substance in Rieti (Italy). In addition, the current building complex at the Rieti site is extended as well as new equipment added. B.I.a.2.b - Changes in the manufacturing process of	18/12/2013	n/a		

	the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
IAIN/0001	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	14/06/2013	n/a		