MULTAQ

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/0053	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/07/2024		SmPC and PL	Sections 4.4 and 4.6 of the SmPC were updated to include the information that prior to initiating MULTAQ, the prescriber should confirm that women of childbearing potential are not pregnant, that they should use effective methods of contraception during treatment with MULTAQ and for 7 days after the final dose and that women should be advised not to breastfeed during treatment with MULTAQ and for 7 days (about 5 half-lives) after the final dose.

[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).

IAIN/0054/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	13/05/2024	n/a		
N/0051	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2023		PL	
PSUSA/1180/202207	Periodic Safety Update EU Single assessment - dronedarone	16/03/2023	n/a		PRAC Recommendation - maintenance
T/0049	Transfer of Marketing Authorisation	31/10/2022	21/11/2022	SmPC, Labelling and PL	
IA/0048	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	04/07/2022	n/a		
IA/0047	A.7 - Administrative change - Deletion of manufacturing sites	08/04/2022	21/11/2022	Annex II and PL	
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/11/2021	12/01/2022	PL	
IA/0045	B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold	23/07/2021	n/a		

	increase compared to the originally approved batch size				
IB/0044/G	This was an application for a group of variations. 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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	08/01/2021	12/01/2022	Annex II and PL	
PSUSA/1180/ 201907	Periodic Safety Update EU Single assessment - dronedarone	26/03/2020	02/06/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1180/201907.
R/0042	Renewal of the marketing authorisation.	25/07/2019	19/09/2019	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of MULTAQ in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0039/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered	12/04/2018	n/a		

	elsewhere in this Annex which involve the submission of studies to the competent authority				
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/11/2017	19/09/2019	Labelling and PL	
II/0038	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/10/2017	n/a		
N/0037	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/03/2017	30/10/2017	PL	
PSUSA/1180/ 201607	Periodic Safety Update EU Single assessment - dronedarone	09/03/2017	n/a		PRAC Recommendation - maintenance
II/0035	To update the Risk Management Plan. 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	10/11/2016	30/10/2017	Annex II	
PSUSA/1180/ 201507	Periodic Safety Update EU Single assessment - dronedarone	17/03/2016	n/a		PRAC Recommendation - maintenance
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/09/2015	30/10/2017	PL	

PSUSA/1180/ 201407	Periodic Safety Update EU Single assessment - dronedarone	12/02/2015	n/a		PRAC Recommendation - maintenance
R/0030	Renewal of the marketing authorisation.	24/07/2014	22/09/2014	SmPC and PL	The CHMP recommends that one additional five-year renewal on the basis of pharmacovigilance grounds is required.
IG/0454	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	17/07/2014	n/a		
IB/0029/G	This was an application for a group of variations. 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 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.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method	12/03/2014	n/a		
PSUV/0028	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
PSUV/0027	Periodic Safety Update	19/09/2013	15/11/2013	SmPC and PL	Update of section 4.4 of the SmPC to update the existing warning related to renal failure as follows:

					Larger increases in creatinine after dronedarone initiation have been reported in the postmarketing setting. Some cases also reported increases in blood urea nitrogen, possibly due to hypoperfusion secondary to developing CHF (pre-renal azotaemia). In such cases dronedarone should be stopped (see sections 4.3 and 4.4). In most cases, these effects appear to be reversible upon drug discontinuation. It is recommended to monitor renal function periodically and to consider further investigations as needed. The Package leaflet is updated accordingly. Furthermore, the PI is updated in line with the latest QRD template version 9 and update the list of local representatives in the Package Leaflet. Please also refer to the Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation for PSUV/0027.
T/0025	Transfer of the Marketing Authorisation. Transfer of Marketing Authorisation	20/08/2013	25/09/2013	SmPC, Labelling and PL	Transfer of the Marketing Authorisation to sanofi-aventis groupe.
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/08/2013	15/11/2013	PL	
IG/0314	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	08/07/2013	n/a		
II/0021	Update of section 4.8 of the SmPC in order to update the safety information with information from the literature on vasculitis, including leukocytoclastic	13/12/2012	25/09/2013	SmPC and PL	In an abstract for publication dating April 2012 (Al-Bataineh et al. Dronedarone-induced Henoch-Schonlein Purpura. Journal of Hospital Medicine 2012) a case concerning a 71-

	vasculitis. The Package Leaflet is updated accordingly. Furthermore, the marketing authorisation holder took advantage of this opportunity to bring the PI in line with the latest QRD template version 8.2. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				year-old male patient who developed Schönlein-Henoch purpura within 2 weeks of treatment with dronedarone was presented. Vasculitis or Schönlein-Henoch vasculitis have not been observed during clinical development of the medicinal product and are not listed. Search in the pharmacovigilance database of the marketing authorisation holder since dronedarone launch to 3 April 2012 was also performed using relevant personal track safety such as henoch-Schönlein purpura, Leukocytoclastic vasculitis, Cutaneous vasculitis, Diffuse vasculitis, Haemorrhagic vasculitis, Rheumatoid vasculitis, Vasculitis, Vasculitis gastrointestinal, Vasculitis necrotising, Purpura, Purpura non-thrombocytopenic and Vascular purpura coded using Medical Dictionary for Regulatory Activities, version 14.1. Taking into account that a causal relationship with dronedarone is possible in at least 4 post-marketing cases, that vasculitis is a listed adverse drug reaction for amiodarone, and that 3 non serious cases (out of 3282) in the pool of 5 atrial fibrillation/atrial flutter placebo-controlled studies were considered relevant to assign a frequency, the CHMP recommended an update of the section 4.8 of the SmPC. The marketing authorisation holder proposed and the CHMP agreed to add vasculitis, including leukocytoclastic vasculitis under category “rare” in the adverse drug reactions table. The package leaflet was updated accordingly. Furthermore, the PI is being brought in line with the latest QRD template version 8.2.
IB/0022	C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH	14/11/2012	25/09/2013	SmPC and PL	

II/0020	Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to contraindicate the concomitant use of dronedarone and dabigatran following the results of a phase 1 drug-drug interaction study. The Package Leaflet was updated in accordance. In addition, Annex II (Conditions or restrictions with regard to the safe and effective use of the medicinal product) was updated to reflect the change in the key messages of the Information Card. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	20/09/2012	24/10/2012	SmPC, Annex II and PL	For further information please refer to the scientific conclusion: H-001043-VAR-II-0020-en
II/0018	Update of section 4.8 of the SmPC in order to include information on anaphylactic reactions. The Package Leaflet is updated accordingly. Furthermore, the PI is being brought in line with the latest QRD template version 8.0. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	19/07/2012	30/08/2012	SmPC, Annex II, Labelling and PL	In this type II variation the MAH proposed the inclusion of 'anaphylactic reactions, including angioedema' in section 4.8 of the SmPC with the frequency "rare". The MAH presented an overview of cases of anaphylactic reaction/shock or angioedema from post-marketing surveillance which showed a relatively short time to onset; this is indicative of a causal relation. In addition, one well-documented case with a positive de- and rechallenge was reported. Furthermore, in several cases, the reactions occurred a few days after the introduction of the drug and resolved after dronedarone withdrawal. A similar reaction while on amiodarone had been noticed in one case. The MAH also queried their database for cases of anaphylactic reaction/shock or angioedema reported in clinical trials. Review of these cases did not identify additional information relevant to be reflected in the SmPC. Case reports from all solicited sources did not add relevant

					information to that obtained from the pooled studies. Based on the data presented, the CHMP agrees that a causal relationship between dronedarone and anaphylactic reactions is likely, and agrees to the frequency proposed by the MAH. The risk of infrequent anaphylactic reactions is still outweighed by the demonstrated benefits of Multaq. Therefore, the overall benefit-risk balance of Multaq remains positive.
IAIN/0019	A.1 - Administrative change - Change in the name and/or address of the MAH	26/04/2012	30/08/2012	SmPC, Labelling and PL	
IG/0147/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	29/02/2012	n/a		

IB/0016	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	11/01/2012	n/a		
A20/0005	Pursuant to Art. 20 of Regulation (EC) No. 726/2004, the European Commission requested the CHMP to re-evaluate the benefit-risk balance of Multaq in light of newly available data on the cardiovascular, hepatic and pulmonary risks, and to give its opinion on whether the marketing authorisation in the approved indication should be maintained, varied, suspended or revoked.	22/09/2011	22/12/2011	SmPC, Annex II and PL	Please refer to the assessment report: EMEA/H/C/1043/A-20/005
II/0012/G	This was an application for a group of variations. To propose an alternative manufacturing process for the synthesis of the active substance; To change some of the specifications for a specific intermediate in the synthesis of the active substance; To replace the test procedure for a specific intermediate in the synthesis of the active substance; B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates,	22/09/2011	22/09/2011		

	which may have a significant effect on the quality of the AS and/or the FP B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue 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.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or				

	replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue				
II/0010	Update of sections 4.4 and 4.5 of the SmPC to include information regarding INR monitoring in patients initiating dronedarone that are undergoing vitamin K antagonists treatment. Subsequently section 2 of the PL and Annex II were updated to reflect the agreed wording. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	23/06/2011	24/08/2011	SmPC, Annex II and PL	The proposed additions in sections 4.4 and 4.5 concerned the interaction of dronedarone and vitamin K antagonists (VKA) and the need to monitor INR in case dronedarone is initiated in patients administered VKA. To support these changes the following three sources of data were analysed: (1) clinical pharmacology data from PK study INT3353, (2) postmarketing data and (3) the data from the clinical studies (DIONYSOS and ATHENA). In particular, the clinical overview containing a cumulative review of post marketing adverse event reports for any cases involving dronedarone and clinically significant increases in INR, and bleeding events or adverse events suggesting higher than required levels of anticoagulation was assessed. This was in addition to post-hoc analyses on the effects of dronedarone on INR in patients treated with OCA performed on the databases from the ATHENA, and DIONYSOS clinical trials comparing dronedarone to placebo and amiodarone, respectively. Following the assessment sections 4.4 and 4.5 were updated to include the warnings that clinically significant INR elevations (≥5) usually within 1 week after starting dronedarone were reported in patients taking OCA and that therefore INR should be closely monitored after initiating dronedarone in patients taking VKA.
II/0004	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	19/05/2011	18/07/2011	SmPC, Annex II and PL	Based on the results of the DDI study INT11479 between dabigatran and dronedarone, the MAH proposed an update in sections 4.4 and 4.5. Study INT11479 showed that there is indeed a pharmacokinetic interaction between dronedarone

					and dabigatran etexilate. Repeated oral doses of dronedarone at 400 mg BID increased the Cmax and AUC0-24 of dabigatran after repeated oral doses of dabigatran at 150 mg OD by 1.73-fold (90% CI: 1.54 to 1.93-fold) and 1.99-fold (90% CI: 1.79 to 2.21-fold), respectively. The pharmacodynamic measurements confirmed this finding, a 1.5 fold increase of the ecarin clotting time (ECT) profile of dabigatran was observed when the drugs were co administered, which is consistent with the observed PK interaction. The effect was less pronounced for the activated thromboplastin time (aPTT), only a 13% increase of the aPTT profile of dabigatran was observed. Overall the study medications were well tolerated. One case of haematuria was reported, which was considered a violation of exclusion criteria. As the number of subjects is limited no definite conclusions can be drawn on the clinical relevance of these findings. Based on the findings from the above mentioned study and in view of no robust clinical data related to this interaction the CHMP agreed that the combined use of dronedarone and dabigatran can not be recommended. In accordance with the SmPC update, the MAH is requested to include the interaction in the RMP as an potential risk risk and to update the Multaq Information Card (MIC).
IG/0091	C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	05/07/2011	n/a		
II/0007/G	This was an application for a group of variations. This was an application for a group variation	14/04/2011	07/06/2011	SmPC and Annex II	To update Annex IIB to include new key safety message on hepatic monitoring prior to and during treatment with dronedarone following the SmPC update within the safety

	consisting of type II and type IA variations. To update Annex IIB to include new key safety message on hepatic monitoring prior to and during treatment with dronedarone following the SmPC update within the safety variation IB/006 and as suggested in AR for FUM 023. To update the SmPC with the ATC code for dronedarone published in the WHO index of January 2011. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH A.6 - Administrative change - Change in ATC Code/ATC Vet Code				variation IB/006 and as suggested in AR for FUM 023. To update the SmPC with the ATC code for dronedarone published in the WHO index of January 2011.
IB/0011/G	This was an application for a group of variations. B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	30/05/2011	n/a	Annex II and PL	

	site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing				
IA/0009	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 currently approved batch size	13/04/2011	n/a		
IA/0008	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	24/03/2011	n/a		
IB/0006	C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH	31/01/2011	n/a	SmPC and PL	To implement changes affecting the product information requested and agreed on by the CHMP further to the assessment Information on two liver transplantation cases. In Section 4.2. "Posology and method of administration" - The hepatic impairment paragraph is updated with a reference to section 4.4. In Section 4.4. "Special warnings and precautions for use" is updated as follow: Addition of a warning for patients regarding liver injury. Section 4.8. "Undesirable effects" - Table 1 is updated with "liver function test abnormalities" and "hepatocellular liver injury, including life-threatening acute liver failure (see section 4.4)"as ADR, with the appropriate frequencies. These changes also impact the package leaflet.

II/0003/G	This was an application for a group of variations. This was an application for a group of 7 type II variations (C.I.4) to update sections 4.3, 4.4, 4.5 and 5.2 of the Annex I to include the information from: 2 in vitro interaction studies (one with the human uptake transporters OATP1B1, OATP1B3, OCT1 and OAT3 in recombinant cell lines and one with human MAO A and B) and 5 in vivo interaction studies (with erythromycin, atorvastatin and rosuvastatin, metformin, omeprazole and clopidogrel). The assessment of some of these studies was performed earlier within FUMs 4, 5, 6, 7-10. Consequently, section 2 of the Annex IIIB was updated. In addition the MAH took the opportunity to make editorial changes in Annex IIIA to correct the initial error in the description of one blister, to make small editorial corrections in Annex IIIB, to update Sections 4.2, 4.6 of Annex I and Annex II and IIIB according to the QRD template v.7.3.1 and to update the list of the local representatives in Annex IIIB. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-	16/12/2010	21/01/2011	SmPC, Annex II, Labelling and PL	

	clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
II/0002	Update of sections 4.4 and 4.8 of Annex I and Section 4 of Annex IIIB to introduce the warning regarding the new onset congestive heart failure, aggravation of congestive heart failure and the congestive heart failure as adverse drug reaction following the CHMP recommendations included in the assessment of the 1st PSUR. In addition version number of the pharmacovigilance system was deleted from Annex II. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	16/12/2010	21/01/2011	SmPC, Annex II and PL	
IA/0001/G	This was an application for a group of variations. To increase the batch size of intermediate in Sanofie Chimie Neuville/Saone site :	03/06/2010	n/a		

	Step 1: input of SR28043 550kg to 910kg (previously 550kg to 800kg) Step 2: input of SR33581 275kg to 1300kg (previously 275kg to 1080kg) To increase the batch size of active substance in Sanofie Chimie Sisteron site: Step 3: input of SR33580A 800kg to 1500kg (previously 800kg to 1100kg) Step 4: synthesis of SR33589B pure 600kg to 1245kg (previously 600kg to 940kg) Standard batch size of drug substance: Sisteron 770kg +/- 130kg or 1150kg +/- 250kg 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 currently approved batch size 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 currently approved batch size				
IG/0004/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the	06/05/2010	n/a	Annex II	

	back-up procedure of the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				