Dukoral

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
IA/0067	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	31/01/2022	n/a		
IB/0066/G	This was an application for a group of variations.	25/05/2021	n/a		

[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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

	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.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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)				
IB/0065	B.II.d.1.b - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits for medicinal products subject to OCABR	03/05/2021	n/a		
PSUSA/730/202004	Periodic Safety Update EU Single assessment - cholera vaccine (inactivated, oral)	14/01/2021	n/a		PRAC Recommendation - maintenance
II/0062/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 A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	17/09/2020	07/01/2021	SmPC, Annex II, Labelling and PL	

	B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation				
IB/0061	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	18/01/2020	n/a		
IB/0060/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.e.5.b - Implementation of changes foreseen in an approved change management protocol - Requires further supportive data	01/08/2019	16/07/2020	SmPC and Annex II	
IB/0059	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	13/02/2019	n/a		
II/0058	Update of the 'instructions for use' in the Package Leaflet in order to increase clarity and reduce the risk of medication errors. Minor corresponding editorial changes have been implemented in section 4.2 of the SmPC. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with	19/07/2018	04/07/2019	SmPC, Annex II, Labelling and PL	n/a

	the latest QRD template version 10, to update Annex II with regards to PSUR requirements, to correct the description of the container of the vaccine suspension and to introduce minor linguistic and layout improvements to the Annexes. C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation				
IB/0057/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.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	04/01/2018	n/a		
PSUSA/730/201704	Periodic Safety Update EU Single assessment - cholera vaccine (inactivated, oral)	30/11/2017	n/a		PRAC Recommendation - maintenance
IA/0056/G	This was an application for a group of variations. B.I.c.1.z - Change in immediate packaging of the AS -	27/10/2017	n/a		

	Other variation B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
IA/0053	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	15/12/2016	n/a		
IB/0052	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	03/06/2016	n/a		
IAIN/0051/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.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.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.7 - Administrative change - Deletion of manufacturing sites	16/03/2015	08/04/2015	SmPC, Annex II, Labelling and PL	
IAIN/0050	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV	26/02/2015	n/a		

	(including contact details) and/or changes in the PSMF location				
IB/0049/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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.d.1.b.1 - Stability of AS - Change in the storage conditions - Change to more restrictive storage conditions of the AS	13/01/2015	n/a		
PSUV/0046	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
IA/0048	A.7 - Administrative change - Deletion of manufacturing sites	10/11/2014	n/a		
IB/0047/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.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	05/11/2014	n/a		

	the AS -replacement or addition of a site where batch control/testing takes place				
II/0045	Update of sections 4.6 and 5.1 of the SmPC to include effectiveness data from two vaccination campaigns (in Mozambique and Zanzibar). Furthermore the MAH took the opportunity of this variation to revise section 4.2 to add the possibility to use chlorinated water to prepare the buffer solution (used in the Mozambique vaccination campaign, according to WHO guidance) and to clarify information regarding the booster for children. Minor changes are made throughout the Product Information which is also updated according to the QRD template version 9. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/09/2014	08/04/2015	SmPC, Annex II, Labelling and PL	The vaccine effectiveness of two doses of Dukoral in the mass vaccination campaigns in Mozambique and Zanzibar of 84% and 78%, respectively, are in the magnitude of the vaccine efficacy in the registrational studies in Bangladesh and Peru. The data are considered valuable from a public health perspective in areas where cholera may be epidemic. No significant harmful effects of non-intended gestational exposure to Dukoral were detected in the vaccination campaign in Zanzibar. The Product Information has been updated to reflect these data, as well as the possibility to use chlorinated water to prepare the buffer solution .
II/0043	Introduction of a post approval change management protocol related to the AS B.I.e.2 - Introduction of a post approval change management protocol related to the AS	26/06/2014	n/a		
IA/0044	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	06/06/2014	n/a		
IB/0042	B.II.f.1.d - Stability of FP - Change in storage	30/04/2014	08/04/2015	SmPC,	

	conditions of the finished product or the diluted/reconstituted product			Labelling and PL	
IAIN/0040	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/07/2013	n/a		
IAIN/0039	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/05/2013	n/a		
II/0038/G	This was an application for a group of variations. This was an application for a group of variations: change in the manufacturing process of the active substance and change to an approved test procedure. 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 medicinal product and is not related to a protocol B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	21/02/2013	n/a		
IB/0037	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	09/01/2013	n/a		
IB/0036	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	19/10/2012	n/a		

IB/0035	B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products	12/09/2012	n/a		
IA/0034/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS B.III.1.b.2 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	23/07/2012	n/a		
II/0033	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	19/04/2012	n/a		

	biological/immunological product				
II/0032	Change in the immediate packaging of the active substance. B.I.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs	20/10/2011	20/10/2011		
IA/0031	B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing	19/05/2011	n/a		
II/0027/G	This was an application for a group of variations. Dukoral batches will be formulated using a higher content of bacteria, 125x109 compared to 100x109 bacteria per vaccine dose. The antigen content stays within the approved range which has proved efficacious and safe in a large number of clinical trials conducted with Dukoral and the dosage is not affected. The reason for this change is to give a greater assurance that the product fully meets the potency requirements over the entire shelf life. As a consequence of this recalibration the Product Information (SmPC, Labelling and PL) has been updated accordingly to reflect the change in the bacterial content prior to inactivation. B.II.b.3.e - Change in the manufacturing process of the finished product - Introduction or increase in the	20/01/2011	21/02/2011	SmPC, Labelling and PL	These variations concerns an introduction of an increase of 25% of the bacterial content (as measured before inactivation) in the manufacture of the finished product and correction of the lipopolysaccharide (LPS) limits at release and during shelf life of the finished product due to reassignment of the LPS content (O1-LPS inhibition ELISA) in a new standard preparation. Dukoral batches will be formulated using a higher content of bacteria, 125x109 compared to 100x109 bacteria per vaccine dose. The antigen content stays within the approved range which has proved efficacious and safe in a large number of clinical trials conducted with Dukoral and the dosage is not affected. The reason for this change is to give a greater assurance that the product fully meets the potency requirements over the entire shelf life. As a consequence of this recalibration the Product Information (SmPC, Labelling and PL) has been updated accordingly to reflect the change in the bacterial content prior to inactivation.

	overage that is used for the AS B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation				
IB/0030	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	26/01/2011	n/a		
IB/0029/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.II.a.3.b.6 - Changes in the composition (excipients) of the finished product - Other excipients - Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level	20/01/2011	n/a	SmPC	
IA/0028/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name	26/11/2010	n/a		

	and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites				
IB/0026	Change in the test procedure for Rifampicin sensitivity and Ampicillin sensitivity. The Working Seed Lot (WSL) will be measured by Optical Density (OD). B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	12/05/2010	n/a		
IB/0025	Change in the Rifampicin sensitivity specification of the WSL. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	12/05/2010	n/a		
IA/0024	A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	06/04/2010	n/a	Annex II	
IA/0023	A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	06/04/2010	n/a	Annex II and PL	
IA/0022	A.1 - Administrative change - Change in the name	06/04/2010	n/a	SmPC,	

	and/or address of the MAH			Labelling and PL	
II/0021	Change in the specifications of the active substance. 14_Change in specifications of active substance	18/03/2010	23/03/2010		
IB/0018	IB_38_c_Change in test procedure of finished product - other changes	30/10/2009	n/a		
IA/0020	IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	30/10/2009	n/a		
IA/0019	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	30/10/2009	n/a		
II/0016	Addition of a site for finished product and active substance testing and change in the name of the manufacturer of the effervescent buffer granules supplied in the finished product. Quality changes	23/04/2009	12/05/2009		
R/0015	Renewal of the marketing authorisation.	22/01/2009	25/03/2009	SmPC, Annex II, Labelling and PL	
II/0014	The Marketing Authorisation Holder applied to change specfications for both finished product and monovalent bulks. Change(s) to the test method(s) and/or specifications	25/09/2008	01/10/2008		

	for the finished product				
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/08/2008	n/a	Labelling	
II/0012	Change(s) to the manufacturing process for the active substance	15/11/2007	23/11/2007		
II/0011	Change(s) to the test method(s) and/or specifications for the active substance	19/07/2007	24/07/2007		
II/0010	Update of Summary of Product Characteristics, Labelling and Package Leaflet	23/06/2005	16/08/2005	SmPC, Labelling and PL	Reformatting of section 4.8 "Undesirable effects" of the Summary of Products Characteristics (SPC) in accordance with MedDRA version 6.0. The Marketing Authorisation Holder (MAH) also took this opportunity to update the Product Information (PI) according to the latest version of the EMEA/ QRD template.
IA/0009	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	14/01/2005	n/a	Annex II	
N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/12/2004	n/a	Labelling and PL	
II/0006	Change(s) to the manufacturing process for the active substance	21/10/2004	25/10/2004		
II/0005	Change(s) to the manufacturing process for the active substance	21/10/2004	25/10/2004		
IB/0001	IB_10_Minor change in the manufacturing process of the active substance	22/07/2004	n/a		
