Liprolog

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
N/0157	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/01/2023	n/a	PL	
WS/2288	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	17/11/2022	n/a		Not applicable

[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).

	Please refer to the Recommendations section B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS				
WS/2285/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. Please refer to the Recommendations section B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	14/07/2022	n/a		Not applicable
WS/2264	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	30/06/2022	n/a		Not applicable

	Please refer to the Recommendations section 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				
PSUSA/1755/ 202104	Periodic Safety Update EU Single assessment - insulin lispro	02/12/2021	n/a		PRAC Recommendation - maintenance
N/0152	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/09/2021		PL	
WS/2115	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/09/2021	n/a		
IB/0150	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	21/04/2021	n/a		
IB/0148	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	31/03/2021	n/a		

IB/0149/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	08/03/2021	n/a		
IB/0147/G	This was an application for a group of variations. B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	29/01/2021	n/a		
IB/0146/G	This was an application for a group of variations.	22/12/2020	n/a		

	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
PSUSA/1755/ 202004	Periodic Safety Update EU Single assessment - insulin lispro	26/11/2020	n/a		PRAC Recommendation - maintenance
IB/0145	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	23/09/2020	n/a		
WS/1909	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	04/09/2020	23/09/2021	SmPC and PL	
IG/1267	B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new	06/07/2020	n/a		

	specification parameter to the specification with its corresponding test method				
WS/1700/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.1.d - Replacement or addition of a manufacturing site for the FP - Site which requires an initial or product specific inspection B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	17/04/2020	n/a		
X/0130	Annex I_1.(c) Replacement of a biological AS with one of a slightly different molecular structure	14/11/2019	16/01/2020	SmPC, Annex II and PL	
IB/0140	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	23/08/2019	n/a		
WS/1620	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.1.a.3 - Change in immediate packaging of the	25/07/2019	n/a		

	finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products				
IB/0139	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	22/07/2019	n/a		
WS/1541	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.1.z - Change in immediate packaging of the finished product - Other variation	27/06/2019	n/a		
WS/1596	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/06/2019	n/a		
IB/0138	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	28/05/2019	n/a		

IB/0135	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	22/05/2019	n/a		
IAIN/0137	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	29/04/2019	16/01/2020	SmPC, Labelling and PL	
IB/0132	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	19/02/2019	n/a		
WS/1537/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.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	24/01/2019	n/a		
IB/0131	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a	04/01/2019	n/a		

	biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)				
IG/1025	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	06/12/2018	n/a		
IG/1007	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	16/11/2018	n/a		
WS/1356/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.e.5.b: To delete the BASAL presentations: EU/1/96/007/010, 029, 037 and 038 for Humalog Basal and EU/1/01/195/022, 023, 026 and 027 for Liprolog Basal. C.I.4: Update of sections 4.2 and 6.6 of the SmPC of Humalog/Liprolog in pre-filled pens and cartridges to address the PRAC recommendation regarding the potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia. In addition, the Worksharing applicant (WSA) took the opportunity to combine all SmPCs resulting in four SmPCs: 100 units/ml presentations, Mix 25 100	17/05/2018	12/02/2019	SmPC, Annex II, Labelling and PL	The product information has been updated to address the PRAC recommendation regarding the potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia and to add the recommendation to only use Lilly insulin cartridges in with Lilly reusable pens. In addition, the MAH has included in section 6.6 of the SmPC the recommendation that Humalog cartridges are to be used with a Lilly reusable insulin pen and should not be used with any other reusable pen as the dosing accuracy has not been established with other pens and that Liprolog cartridges are to be used with a Lilly reusable insulin pen and should not be used with any other reusable pen as the dose accuracy has not been established with other pen. The Basal presentation has also been deleted from the marketing authorisation. As a consequence of this application the labelling and package leaflet have been updated.

	units/ml presentations, Mix50 100 units/ml presentations and 200 units/ml presentations. The MAH also brought the product information in line with the latest QRD template version 10, 02/2016, and included the recommendation to only use Lilly insulin cartridges with Lilly reusable pens. Minor editorial changes have been included. The Package Leaflet and Labelling are updated accordingly. B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s) C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0126/G	This was an application for a group of variations. B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	12/04/2018	n/a		
WS/1314	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.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative	01/02/2018	12/02/2019	SmPC	

	composition - Sterile medicinal products and biological/immunological medicinal products				
PSUSA/1755/ 201704	Periodic Safety Update EU Single assessment - insulin lispro	30/11/2017	n/a		PRAC Recommendation - maintenance
WS/1158/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.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.IV.1.c - Change of a measuring or administration device - Addition or replacement of a device which is an integrated part of the primary packaging C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/09/2017	23/10/2017	SmPC, Annex II, Labelling and PL	
IG/0846	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	04/10/2017	n/a		
WS/1226	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.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative	14/09/2017	n/a		

	composition - Sterile medicinal products and biological/immunological medicinal products				
WS/1188	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final report of a non-interventional post-authorisation safety study EUPAS 13422. This study is aimed to evaluate the impact of additional risk minimisation measures on healthcare professionals and on patients' understanding and their behaviour regarding the risk of hypoglycaemia and/or hyperglycaemia due to medication errors associated with administration of Humalog 200 U/ml KwikPen. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/09/2017	n/a		
IB/0118	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	24/03/2017	n/a		
IAIN/0119/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within	16/03/2017	23/10/2017	SmPC, Annex II, Labelling and PL	

	the range of the currently approved pack sizes				
WS/1061/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.1.c (Type II): To add a new site (Eli Lilly Italia SpA, Via Gramsci, 731-733, 50019 Sesto Fiorentino, Italy) for the manufacture of Humalog and Liprolog 200U/mL, 3.0 mL cartridges. B.II.b.2.c.2 (Type IB): To add a new site (Eli Lilly Italia SpA, Via Gramsci, 731-733, 50019 Sesto Fiorentino, Italy) for the quality control testing and batch release of Humalog and Liprolog 200U/mL, 3.0 mL cartridges. The addition of the new facility results in some consequential changes to the manufacturing process in this new site: B.II.b.4 a (Type IB): to add a new 1250L batch size. B.II.b.5 b (Type IA): to add a new in-process control test method (the post filtration filter integrity test) with its test limits. 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	15/12/2016	23/10/2017	Annex II and PL	

	B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing 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 B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits				
WS/1024	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)	15/12/2016	n/a		
IB/0116	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	23/11/2016	n/a		
WS/1054	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	10/11/2016	23/10/2017	SmPC, Annex II, Labelling and PL	
IB/0114	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	19/10/2016	n/a		

WS/0962/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.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	21/07/2016	n/a		
IB/0110	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	03/06/2016	n/a		
IB/0108/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished	09/03/2016	n/a		

	product - Deletion of a non-significant in-process test B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method				
IG/0662	A.1 - Administrative change - Change in the name and/or address of the MAH	23/02/2016	26/05/2016	SmPC, Labelling and PL	
WS/0879/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.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.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	28/01/2016	n/a		
WS/0844/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.3.a - Change in the manufacturing process of	28/01/2016	n/a		

	the finished or intermediate product - Minor change in the manufacturing process B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method				
WS/0855/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.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	17/12/2015	n/a		
IB/0103	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/12/2015	26/05/2016	SmPC, Annex II and PL	
IG/0641	A.7 - Administrative change - Deletion of manufacturing sites	09/12/2015	n/a		

IG/0567	A.7 - Administrative change - Deletion of manufacturing sites	20/05/2015	26/05/2016	Annex II and PL	
IB/0100	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	05/05/2015	n/a		
WS/0679	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	26/02/2015	n/a		
IG/0515	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	15/12/2014	n/a		
PSUV/0095	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
X/0092	Addition of a a new strength: 200 U/ml Annex I_2.(c) Change or addition of a new strength/potency	24/07/2014	01/10/2014	SmPC, Labelling and PL	Please refer to the scientific discussion Liprolog EMEA/H/C/000393/X/0092 for further information.
IB/0096/G	This was an application for a group of variations. B.I.d.1.a.1 - Stability of AS - Change in the re-test period/storage period - Reduction B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a	30/09/2014	n/a		

	biological/immunological medicinal product B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product				
IG/0455	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	08/07/2014	01/10/2014	Annex II and PL	
IB/0093	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/04/2014	01/10/2014	SmPC and PL	
WS/0353/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. Post-approval change management protocols to introduce changes to the manufacture of the active substance. B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS	20/02/2014	n/a		
IB/0091	C.I.z - Changes (Safety/Efficacy) of Human and	14/11/2013	01/10/2014	SmPC, Annex	

	Veterinary Medicinal Products - Other variation			II, Labelling and PL	
IG/0363	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	16/10/2013	n/a		
IG/0362/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 alternative method is already authorised B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier 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 B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	11/10/2013	n/a		
N/0085	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/09/2013	01/10/2014	PL	
IB/0087/G	This was an application for a group of variations. B.V.c.1.c - Change management protocol - Update of the quality dossier to implement changes, requested by the EMA/NCA, following assessment of a change management protocol - Implementation of a change	05/09/2013	n/a		

	for a biological/immunological medicinal product B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation				
IG/0337	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	09/08/2013	n/a		
IG/0321	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/07/2013	n/a		
IB/0084	B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	16/04/2013	n/a		
IB/0083	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	22/03/2013	n/a		
IB/0082	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	01/03/2013	n/a		
WS/0335/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. This application is a grouped Type II variation:	13/12/2012	n/a		

	- to add an additional manufacturing site for Insulin Lispro Mix 50 cartridges. - to change the manufacturing process (equipment changes, change in batch size) - to change the in-process tests or limits applied during the manufacture of the finished product 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, batch control, and secondary packaging, for biological/immunological medicinal products. B.II.b.3.c - Change in the manufacturing process of the finished product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				

IB/0079	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	16/11/2012	n/a		
IB/0076/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing	10/08/2012	25/10/2012	Annex II and PL	
IB/0077	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	26/06/2012	n/a		
IB/0075	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	13/04/2012	n/a		
IB/0074	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	13/04/2012	25/10/2012	SmPC	

WS/0196/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. Changes to in-process tests B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS B.I.a.4.f - Change to in-process tests or limits applied during the manufacture of the AS - Addition or replacement of an in-process test as a result of a safety or quality issue	15/03/2012	n/a		
IB/0070	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	02/12/2011	n/a		
II/0065/G	This was an application for a group of variations. -To change the batch size of an intermediate.	21/07/2011	21/07/2011		

	-To add a new in-process test or limit in the manufacture of the active substance. -To introduce a change in the manufacturing process of the active substance. -To change the specification parameters or limits of the active substance. -To replace a test procedure for a reagent. 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.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
N/0069	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/07/2011	25/10/2012	PL	

II/0067	Changes to manufacturing processes at one site to mirror those at another site doing the same manufacturing processes. B.II.b.3.c - Change in the manufacturing process of the finished product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	23/06/2011	23/06/2011		
WS/0111	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Further to a review of safety information pertaining to the risk of fluid retention and congestive heart failure with the use of insulin lispro, section 4.8 of the Summary of Product Characteristics (SmPC) is updated by adding a warning on an increased incidence of oedema. The Package Leaflet section 4 is updated accordingly. This application was submitted for a group of variations consisting of Type II variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/03/2011	20/04/2011	SmPC and PL	Review of the safety information from Lilly Safety System and literature data sources pertaining to the risk of fluid retention (including oedema and peripheral oedema) with the use of insulin lispro suggests a causal association between insulin lispro and the adverse event of oedema. Therefore it was proposed to provide information regarding oedema in the adverse event sections of the product information. Analysis of the patients exposed to insulin lispro between 1 January 1983 through 31 August 2010 confirmed causal association between insulin lispro and the adverse event of oedema. Consequently Summary of Product Characteristics section 4.8 is updated by adding a warning on an increased incidence of oedema. It was agreed not to mention frequency as the majority of the reports occur within the first weeks of treatment. The Package Leaflet section 4 is updated accordingly.
WS/0105	This was an application for a variation following a	17/02/2011	17/03/2011	SmPC, Annex	The PhVWP was requested to consider whether the

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Further to a CHMP request based on the recommendations from PhVWP, the Product Information (Summary of Product Characteristics section 4.4 and Package Leaflet section 2) is updated by adding a warning on an increased incidence of heart failure when pioglitazone is used in combination with insulin, especially in patients with predisposing factors. In addition to the above the MAH took the opportunity to update annex IIB "Other conditions" for Liprolog with the latest wording as per October 2010 CHMP announcment regarding the Pharmacovigilance system. This application was submitted for a group of variations consisting of Type IB variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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			II and PL	increased risk of fluid retention and exacerbation of heart failure with the concomitant use of pioglitazone and insulin should apply to all centrally authorised insulin products. After the review of the available evidence, during its October 2010 meeting the PhVWP has concluded this review with a recommendation to the CHMP on the need to harmonise the SmPC and PL for all insulin products by including appropriate warning. The CHMP endorsed this recommendation, and in this context the Committee agreed that all centrally authorised insulin containing products should include warning on increased cardiac failure when pioglitazone is used in combination with insulin, especially in patients with predisposing factors in the in the section 4.4 of the SmPC and section 2 of the PL.
IA/0066/G	This was an application for a group of variations. C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the	23/02/2011	n/a		

	major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD 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				
II/0063/G	This was an application for a group of variations. Change in the manufacturinng process of finished product. Change to in-process test of finished product. B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	18/11/2010	25/11/2010		
IB/0064	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	27/09/2010	n/a		
II/0061	B.II.b.3b) Change in the manufacturing process of the finished product.. Substantial changes to a	24/06/2010	30/06/2010		

	manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product. B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product				
IB/0060	To increase the batch size of the finished product. B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	25/06/2010	n/a		
N/0062	The Marketing Authorisation Holder took the opportunity to update the User Manual for Liprolog KwikPens. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/04/2010	n/a	PL	
II/0058	Change in the re-test period of the active substance. Update of or change(s) to the pharmaceutical documentation	18/03/2010	23/03/2010		
IB/0059	IB_31_a_Change to in-process tests/limits during	28/01/2010	n/a		

	manufacture - tightening of in-process limits				
IA/0057	To change a method of analysis for the active substance to comply with Ph. Eur. IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance	26/11/2009	n/a		
N/0056	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/10/2009	n/a	PL	
II/0053	Change(s) to the manufacturing process for the finished product	23/07/2009	18/08/2009		
IB/0055	IB_30_b_Change in supplier of packaging components - replacement/addition	11/08/2009	n/a		
II/0049	Update of sections 4.5, 6.3 and 6.4 of the Summary of Product Characteristics and of the relevant sections of the Package Leaflet (PL). Update of Summary of Product Characteristics and Package Leaflet	29/05/2009	01/07/2009	SmPC and PL	Further the assessment of the PSUR covering the period from 01 May 2005 to 30 April 2008, the CHMP recommended the update of the following sections of the SPC: - section 4.5 to include SSRIs (Selective Serotonin Reuptake Inhibitors) as potential hypoglycaemic antidepressants - sections 6.3 and 6.4 in order to improve the storage instructions. The package leaflet has been updated accordingly.
IB/0054	IB_37_a_Change in the specification of the finished product - tightening of specification limits	28/05/2009	n/a		

IB/0052	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	26/05/2009	n/a	SmPC	
IA/0051	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	04/05/2009	n/a		
N/0050	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/04/2009	n/a	Labelling	
II/0046	Update of section 4.2 of the SPC for Liprolog Basal. Update of Summary of Product Characteristics	19/03/2009	22/04/2009	SmPC	This variation consists in the deletion of the following wording concerning the use of Liprolog Basal with other antidiabetic agents: "Liprolog Basal may be used alone, in combination with oral agents, or mixed with insulin lispro solution. In intensive insulin therapy, Liprolog Basal may be used as a basal insulin (evening and/or morning injection) in combination with fast-acting insulin (given at meals)."
IA/0048	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	08/12/2008	n/a		
IA/0047	IA_09_Deletion of manufacturing site	19/09/2008	n/a	Annex II and PL	
IA/0045	The Marketing Authorisation Holder applied to add an alternative site for the batch release of the finished product. IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	02/09/2008	n/a	Annex II and PL	
X/0039	Annex I_2.(a) Change of bioavailability	24/04/2008	11/07/2008	SmPC, Labelling and	

				PL	
II/0043	Change(s) to the manufacturing process of the finished product. Change(s) to the manufacturing process for the finished product	26/06/2008	02/07/2008		
II/0042	Change(s) to the manufacturing process of the active substance. Change(s) to the manufacturing process for the active substance	26/06/2008	01/07/2008		
IA/0044	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	18/04/2008	n/a		
IB/0041	IB_37_b_Change in the specification of the finished product - add. of new test parameter	05/03/2008	n/a		
N/0038	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/02/2008	n/a	Labelling and PL	
II/0037	New presentation(s)	13/12/2007	29/01/2008	SmPC, Annex II, Labelling and PL	
IA/0040	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	28/01/2008	n/a		
IA/0036	IA_28_Change in any part of primary packaging material not in contact with finished product	10/08/2007	n/a		

II/0035	Update of section 4.5 of the SPC and Package Leaflet to add angiotensin II receptor blockers in the list of medicinal products that may reduce insulin requirements. The details of local representatives are updated. Update of Summary of Product Characteristics and Package Leaflet	22/03/2007	02/05/2007	SmPC and PL	The MAH reviewed their safety database over the period 01 January 1983 - 28 February 2005. No suspected interaction with an angiotensin II receptor blockers (ARB) was reported. However, the review of the safety database showed a slight increased frequency of hypoglycaemic events in patients receiving an ACE inhibitor or an Angiotensin Converting Enzyme (ARB) as concomitant medication, which supports a possible interaction with insulin. Although the overall number of reports is lower with ARBs than with ACE inhibitors, the reporting rate appears to be the same. Although the mechanism of the interaction is not well understood, both types of medicinal products share the similar endpoint to decrease the effect of angiotensin II and thus, both have the potential to increase insulin sensitivity. A published clinical study comparing the effects of an ACEI and an ARB showed more pronounced effects of the ACE inhibitors on endothelial function but similar effects on insulin sensitivity (Am J Hypertens. 2005 Feb;18(2 Pt 1):178-82) and thus support the data from the MAH safety database. Therefore section 4.5 of the SPC was updated to include ARBs in the list of medicinal products that may reduce insulin requirements
II/0032	Change(s) to the manufacturing process for the active substance	22/02/2007	27/03/2007	Annex II	
II/0034	Update of SPC sections 4.4 and 5.1 further to the assessment of the FUM 011 to reinforce dosage instructions when using both fast-acting insulins and basal insulins for optimal glucose control, in particular nocturnal/fasting glucose control. In	22/02/2007	14/03/2007	SmPC and PL	The review of the results of three paediatric studies with insulin lispro showed that there were no major differences in overall safety and efficacy between insulin lispro and human regular insulin. However, in two of the studies there were differences concerning fasting and nocturnal blood

	addition, contact details of Bulgarian and Romanian local representatives were also included. Update of Summary of Product Characteristics and Package Leaflet				glucose concentrations with higher concentrations in patients treated with insulin lispro. Therefore, and as recommended by the CHMP, sections 4.4 and 5.1 of the SPC are revised so that all information regarding adjustment of insulin doses can be found in the same section, and to strengthen that a patient also on basal insulin must optimise dosage of both insulins to obtain glucose control across the whole day, particularly nocturnal/fasting glucose control.
IA/0033	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	08/01/2007	n/a		
II/0028	Update of or change(s) to the pharmaceutical documentation	18/10/2006	20/11/2006	Annex II	
II/0030	This variation refers to an update of section 5.1 of the Summary of Product Characteristics to add clinical efficacy information based on the results of two phase IV clinical studies. Update of Summary of Product Characteristics	27/07/2006	01/09/2006	SmPC	The MAH provided the results of two randomized, open-label, crossover studies investigating the efficacy and safety of the combination of twice-daily insulin lispro LM plus metformin and once-daily insulin glargine plus metformin on overall glycaemic control, as measured by % HbA1c. Patients who participated in these studies had type 2 diabetes with inadequately controlled blood glucose, either on one or more oral anti-hyperglycaemic medications only (study IOND, N=74), or on one or more oral anti-hyperglycaemic plus one daily injection of insulin or a conventional insulin regimen consisting of once- or twice-daily NPH insulin (study IOMX, N=93). Results showed that twice-daily insulin lispro LM in combination with metformin has a greater HbA1c-lowering effect than once-daily insulin glargine with metformin, as expressed in mean % HbA1c thereafter. The new data were reflected in section 5.1 of

					the SPC, including those obtained for secondary parameters (blood glucose, frequency of hypoglycaemia, total insulin dose and bodyweight).
IA/0031	IA_28_Change in any part of primary packaging material not in contact with finished product	18/07/2006	n/a		
IB/0029	IB_20_c_Change in test procedure for an excipient - other changes	31/03/2006	n/a		
II/0027	Update of or change(s) to the pharmaceutical documentation	23/02/2006	03/03/2006		
R/0025	Renewal of the marketing authorisation.	14/12/2005	13/02/2006	SmPC, Annex II, Labelling and PL	Based on the review of the available information, the CHMP was of the opinion that the quality, the safety and the efficacy of Liprolog continues to be adequately and sufficiently demonstrated and that the benefit/risk profile of Liprolog continues to be favourable in the treatment of patients with diabetes mellitus. Based on the review of the available information, the CHMP was of the opinion that the quality, the safety and the efficacy of Liprolog continues to be adequately and sufficiently demonstrated and that the benefit/risk profile of Liprolog continues to be favourable in the treatment of patients with diabetes mellitus.
II/0023	Change to the test procedure and/or specification of a raw material	13/10/2005	18/10/2005		
IB/0026	IB_25_a_02_Change to comply with Ph. -	10/10/2005	n/a		

	compliance with EU Ph. - excipient				
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/08/2005	n/a	PL	
II/0022	Change(s) to the manufacturing process for the finished product	26/05/2005	06/06/2005		
II/0021	Change(s) to the test method(s) and/or specifications for the active substance	17/02/2005	23/02/2005		
IB/0020	IB_37_a_Change in the specification of the finished product - tightening of specification limits	06/12/2004	n/a		
II/0018	Update of sections 4.6 and 5.3 of the Summary of Product Characteristics. Update of Summary of Product Characteristics Update of Summary of Product Characteristics and Package Leaflet	16/09/2004	29/10/2004	SmPC and Annex II	The MAH applied to amend the SPC regarding clinical experience with insulin lispro in pregnancy. This claim was based on data from three sources (study F3Z-MC-IONS, Pharmacovigilance data and published literature). The statement "data on a large number of exposed pregnancies do not indicate an adverse effect of insulin lispro on pregnancy or on the health of the foetus/newborn", was included in section 4.6 of the SPC. To be in line with the requirements of the SPC guideline, the MAH also applied to move the preclinical information about embryotoxicity from section 4.6 to section 5.3.
II/0017	Update of sections 6.2 and 6.6 of thr Summary of Product Characteristics and Package Leaflet. Update of Summary of Product Characteristics and Package Leaflet	16/09/2004	29/10/2004	SmPC and PL	The MAH applied for a variation to update sections 6.2 and 6.6 of the SPC and the corresponding sections in the PL to add a warning stating that Liprolog should not be mixed with other insulin products. For some presentations, section 6.6 of the SPC was also updated to clarify that only certain Minimed and Disetronic infusion

					pumps may be used to infuse insulin lispro.
IA/0016	IA_05_Change in the name and/or address of a manufacturer of the finished product	22/06/2004	n/a		
II/0015	Update of or change(s) to the pharmaceutical documentation. Update of or change(s) to the pharmaceutical documentation	03/06/2004	09/06/2004		
II/0014	Update of or change(s) to the pharmaceutical documentation. Update of or change(s) to the pharmaceutical documentation	24/03/2004	30/03/2004		
I/0013	15_Minor changes in manufacture of the medicinal product	20/11/2003	25/11/2003		
X/0012	Addition of a new route of administration. Sections 4.2 and 6.6 of the Summary of Product Characteristics and Package Leaflet were updated. X-3-v_Addition of a new route of administration	24/07/2003	07/11/2003	SmPC, Annex II, Labelling and PL	The MAH submitted an application to include a new route of administration (intravenous use). Until that moment, the authorised route of administration for Liprolog was subcutaneous use. The MAH submitted two studies to support the intravenous use of Liprolog solution for injection (vial, cartridge and pen). The data submitted suggested that Liprolog, given intravenously in circumstances as acute illness or during and after surgery, might be effective and safe in controlling hyperglycaemia in diabetic patients. Sections 4.2 and 6.6 of the SPC and the PL were updated with this information.

II/0011	Update of sections 4.4, 4.5 and 4.6 of the Summary of Product Characteristics. Also to include minor changes in sections 2, 4.2, 4.9, 5.1, 6.1 and 6.6. Update of the Package Leaflet accordingly. Update of Summary of Product Characteristics and Package Leaflet	24/07/2003	07/11/2003	SmPC and PL	The MAH applied for a variation to update section 4.6 of the SPC regarding data from animal studies on fertility impairment, embryotoxicity or teratogenicity. The MAH provided a review of some studies included in the original dossier aiming to evaluate the overall reproductive performance in animals. The studies showed that insulin lispro did not induced fertility impairment, embryotoxicity or teratogenicity in animals. The MAH also applied to include the following sentence in section 5.1 of the SPC: "Insulin lispro has been shown to be equipotent to human insulin on a molar basis but its effect is more rapid and a shorter duration". Previously submitted data from the IMAC study was referred by the MAH to support this claim. Data from IMAC study demonstrated that at different doses, insulin lispro and regular human insulin showed almost identical pharmacokinetics and glucodynamics.Additionally, the MAH applied to update the SPC regarding the concomitant use of Liprolog and monoamine oxidase inhibitors. The reference that certain antidepressants might reduce insulin requirements was updated with monoamine oxidase inhibitors in section 4.5 of the SPC and PL. Three published papers were cited by the MAH as supporting evidence.Conditions which describe warning symptoms of hypoglycaemia were also updated in section 4.4 of the SPC.
II/0010	Update of section 5.1 of the Summary of Product Characteristics. Update of Summary of Product Characteristics	24/07/2003	07/11/2003	SmPC	The MAH applied to include data on reduction of nocturnal hypoglycaemia in section 5.1 of the SPC. To support its claim the MAH provided data from seven clinical studies in patients with Type 1 diabetes, and 2 clinical studies in patients with Type 2 diabetes. On the basis of these studies results, it was concluded that the use of insulin lispro in Type 1 and Type 2 diabetes leads to less nocturnal

					hypoglycaemia than regular insulin. However, in some studies, reduction of nocturnal hypoglycaemia was associated with increased episodes of daytime hypoglycaemia.
II/0009	Update of section 5.1 of the Summary of Product Characteristics. Update of Summary of Product Characteristics	24/07/2003	07/11/2003	SmPC	The MAH applied for a variation to update section 5.1 of the SPC regarding data on the reduction of postprandial hyperglycaemia with insulin lispro and lispro Mix25 compared to soluble human insulin and human insulin Mix30/70 respectively. To support its claim the MAH provided data from five published clinical studies comparing postprandial glucose control with insulin lispro and regular human insulin. The following wording was added to section 5.1 of the SPC for Liprolog: "Clinical trials in patients with Type 1 and Type 2 diabetes have demonstrated reduced postprandial hyperglycaemia with insulin lispro compared to soluble human insulin. For fast acting insulins, any patient also on a basal insulin must optimise dosage of both insulins to obtain improved glucose control across the whole day" and the following sentence was added for Liprolog Mix25: "Clinical trials in patients with Type 1 and Type 2 diabetes have demonstrated reduced postprandial hyperglycaemia with Liprolog Mix25 compared to human insulin mixture 30/70. In one clinical study there was a small (0.38mmol/l) increase in blood glucose levels at night (3.a.m)".
II/0008	Update of sections 4.2 and 5.1 of the Summary of Product Characteristics. Update of Summary of Product Characteristics	24/07/2003	07/11/2003	SmPC	Combination therapy with insulin and sulphonylurea drugs is often used in patients with type 2 diabetes. The MAH applied for a variation to update sections 4.2 and 5.1 of the SPC with current information regarding the use of insulin lispro with sulphonylurea drugs; providing data from two

					studies indicating that insulin lispro is effective and safe when combined with sulphonylurea agents.
I/0007	12_Minor change of manufacturing process of the active substance 12a_Change in specification of starting material/intermediate used in manuf. of the active substance	24/07/2003	03/10/2003		
I/0006	17_Change in specification of the medicinal product	23/05/2003	27/05/2003		
I/0005	30_Change in pack size for a medicinal product	19/02/2003	24/03/2003	SmPC, Labelling and PL	
I/0004	01_Change in the name of a manufacturer of the medicinal product	19/02/2003	24/03/2003	Annex II and PL	
I/0003	30_Change in pack size for a medicinal product	19/02/2003	24/03/2003	SmPC, Labelling and PL	
I/0002	15_Minor changes in manufacture of the medicinal product	25/04/2002	n/a		
II/0001	Quality changes	21/03/2002	16/04/2002		