ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORM, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTE OF ADMINISTRATION, APPLICANTS / MARKETING AUTHORISATION HOLDER IN THE MEMBER STATES

Member State	Marketing Authorisation Holder	Applicant	Name	Strength	Pharmaceutical Form	Route of administration
Austria		Teva Pharma B.V. Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht The Netherlands	Lansoprazol TEVA 15 mg Kapseln	15 mg	Gastro-resistant capsule, hard	Oral use
Austria		Teva Pharma B.V. Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht The Netherlands	Lansoprazol TEVA 30 mg Kapseln	30 mg	Gastro-resistant capsule, hard	Oral use
Belgium		IPS N.V. Jozef Nellenslei 10 – B-2100 Deurne Belgium	Lansoprazol IPS 15 mg maagsapresistente capsules	15 mg	Gastro-resistant capsule, hard	Oral use
Belgium		IPS N.V. Jozef Nellenslei 10 – B-2100 Deurne Belgium	Lansoprazol IPS 30 mg maagsapresistente capsules	30 mg	Gastro-resistant capsule, hard	Oral use
Czech Republic		Teva Pharmaceuticals CR, s.r.o. Drážní 7, 627 00 Brno Czech Republic	Lansoprazol - TEVA 15 mg	15 mg	Gastro-resistant capsule, hard	Oral use
Czech Republic		Teva Pharmaceuticals CR, s.r.o. Drážní 7, 627 00 Brno Czech Republic	Lansoprazol - TEVA 30 mg	30 mg	Gastro-resistant capsule, hard	Oral use
Denmark		Teva Pharma B.V. Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht The Netherlands	Lansoprazol TEVA 15 mg enterokapsler	15 mg	Gastro-resistant capsule, hard	Oral use
Denmark		Teva Pharma B.V. Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht The Netherlands	Lansoprazol TEVA 30 mg enterokapsler	30 mg	Gastro-resistant capsule, hard	Oral use
Finland		Teva Pharma B.V. Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht The Netherlands	Lansoprazol Teva, 15 mg enterokapseli, kova	15 mg	Gastro-resistant capsule, hard	Oral use

Finland	Teva Pharma B.V. Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht The Netherlands	Lansoprazol Teva, 30 mg enterokapseli, kova	30 mg	Gastro-resistant capsule, hard	Oral use
France	TEVA Classics S.A. 1, cours du Triangle, Immeuble Palatin 1, 92936 Paris La Défense cedex 12 France	Lansoprazole TEVA 15 mg microgranules gastro résistantes en gélule	15 mg	Gastro-resistant capsule, hard	Oral use
France	TEVA Classics S.A. 1, cours du Triangle, Immeuble Palatin 1, 92936 Paris La Défense cedex 12 France	Lansoprazole TEVA 30 mg microgranules gastro résistantes en gélule	30 mg	Gastro-resistant capsule, hard	Oral use
Germany	TEVA Generics GmbH Kandelstraße 10, D-79199 Kirchzarten Germany	Lansoprazol-TEVA® 15 mg magensaftresistente Hartkapseln	15 mg	Gastro-resistant capsule, hard	Oral use
Germany	TEVA Generics GmbH Kandelstraße 10, D-79199 Kirchzarten Germany	Lansoprazol-TEVA® 30 mg magensaftresistente Hartkapseln	30 mg	Gastro-resistant capsule, hard	Oral use
Hungary	TEVA Magyarország Rt Rákóczi út 70-72, Budapest, H-1074, Hungary	Lansoflux Teva 15 mg kapszula	15 mg	Gastro-resistant capsule, hard	Oral use
Hungary	TEVA Magyarország Rt Rákóczi út 70-72, Budapest, H-1074, Hungary	Lansoflux Teva 30 mg kapszula	30 mg	Gastro-resistant capsule, hard	Oral use
Ireland	Teva Pharma B.V., Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht, The Netherlands,	Lansoprazole TEVA 15 mg Gastro-resistant Capsules	15 mg	Gastro-resistant capsule, hard	Oral use
Ireland	Teva Pharma B.V., Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht, The Netherlands,	Lansoprazole TEVA 30 mg Gastro-resistant Capsules	30 mg	Gastro-resistant capsule, hard	Oral use

The Netherlands		Pharmachemie B.V. Swensweg 5, Postbus 552, 2003 RN Haarlem The Netherlands	Lansoprazol 15 mg PCH, maagsapresistente capsule	15 mg	Gastro-resistant capsule, hard	Oral use
The Netherlands		Pharmachemie B.V. Swensweg 5, Postbus 552, 2003 RN Haarlem The Netherlands	Lansoprazol 30 mg PCH, maagsapresistente capsule	30 mg	Gastro-resistant capsule, hard	Oral use
United Kingdom	TEVA UK Limited Brampton Road, Hampden Park, Eastbourne, East Sussex, BN22 9AG United Kingdom		Lansoprazole 15 mg Gastro-resistant Capsules	15 mg	Gastro-resistant capsule, hard	Oral use
United Kingdom	TEVA UK Limited Brampton Road, Hampden Park, Eastbourne, East Sussex, BN22 9AG United Kingdom		Lansoprazole 30 mg Gastro-resistant Capsules	30 mg	Gastro-resistant capsule, hard	Oral use

Norway	Teva Pharma B.V., Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht, The Netherlands,	Lansoprazol TEVA 15 mg enterokapseler, harde	15 mg	Gastro-resistant capsule, hard	Oral use
Norway	Teva Pharma B.V., Industrieweg 23, P.O. Box 217, 3640 AE Mijdrecht, The Netherlands,	Lansoprazol TEVA 30 mg enterokapseler, harde	30 mg	Gastro-resistant capsule, hard	Oral use
Poland	Teva Pharmaceuticals Polska Sp. z o.o. E. Plater 53, 00-113 Warsaw Poland	LansoTEVA 15 mg kapsulka dojelitowa twarda	15 mg	Gastro-resistant capsule, hard	Oral use
Poland	Teva Pharmaceuticals Polska Sp. z o.o. E. Plater 53, 00-113 Warsaw Poland	LansoTEVA 30 mg kapsulka dojelitowa twarda	30 mg	Gastro-resistant capsule, hard	Oral use
Slovak Republic	Teva Pharmaceuticals CR, s.r.o. Drážní 7, 627 00 Brno Czech Republic	Lansoprazol - TEVA 15 mg	15 mg	Gastro-resistant capsule, hard	Oral use
Slovak Republic	Teva Pharmaceuticals CR, s.r.o. Drážní 7, 627 00 Brno Czech Republic	Lansoprazol - TEVA 30 mg	30 mg	Gastro-resistant capsule, hard	Oral use
Sweden	TEVA Sweden AB PO Box 1070, SE - 25110 Helsingborg Sweden	Lansoprazol TEVA 15 mg enterokapslar, hårda	15 mg	Gastro-resistant capsule, hard	Oral use
Sweden	TEVA Sweden AB PO Box 1070, SE - 25110 Helsingborg Sweden	Lansoprazol TEVA 30 mg enterokapslar, hårda	30 mg	Gastro-resistant capsule, hard	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF LANSOPRAZOLE AND ASSOCIATED NAMES (see Annex I)

Lansoprazole 15 & 30 mg gastro-resistant capsules, hard (Teva UK Ltd) are generic preparations containing lansoprazole as the active substance. Lansoprazole is a proton pump inhibitor that inhibits gastric acid secretion and is used for the treatment of duodenal and benign gastric ulcers, gastro-oesophageal reflux disease and associated conditions.

In September 2006, a Mutual Recognition Procedure was started for Lansoprazole involving 16 CMS with the UK as Reference Member State (RMS).

On 30 November 2006, the application has been referred and submitted for arbitration according to Article 29 of Directive 2001/83/EC, as amended.

The objecting Concerned Member States raised public health objections on the grounds that while bioequivalence was proven in the fasting state, the same was not the case under fed conditions.

The RMS approved the product on the basis of the results of the fasted study showed unequivocal equivalence as shown by the 90% confidence intervals (CI) for the AUC and C_{max} which were within the conventional 80-125% bioequivalence range. Although the CI for the fed study results (CI for AUCinf. 78–110%) were outside the conventional limits they comply with the wider 75-133% criterion. It was considered that this wider criterion can be applied in this case because of the extremely high intra-subject variability (70- 82%) under fed conditions shown in this study. The results were also considered acceptable on clinical grounds as lansoprazole's efficacy is largely independent of dose at this therapeutic dose range.

Documentation presented to the CHMP shows that the test and reference products are essentially similar. Both products show pronounced food effect although the generic product appears to be more affected largely because of the high intra-subject variability. This is supported by two similar fed studies using the same reference drug and the same test drug with the same batch number when entirely different results are obtained and which confidence intervals were within conventionally acceptable limits.

The results of these fed studies demonstrate that Lansoprazole's bioavailability is not only markedly reduced when taken with food, but that its absorption, in the presence of food, can be very erratic. This is a known pharmacokinetic characteristic of Lansoprazole, particularly when taken with high fat and calorie meal as in the current case.

Lansoprazole has a wide therapeutic window regarding its clinical efficacy and safety. It also has a flat dose/response curve i.e. its efficacy is largely independent of the dose. This means that the small difference in blood levels between the reference and test products shown under fed conditions is of no clinical significance.

In conclusion, the questions have been addressed satisfactorily by the applicant. The Applicant has provided sufficient data to support that the outcome of the fed study does not lead to a potential risk to public health.

The CHMP has recommended the granting of the Marketing Authorisation(s). The valid Summary of Product Characteristics, labelling and package leaflet are the final versions achieved during the Coordination group procedure as mentioned in Annex III.

ANNEX III

SUMMARY OF PRODUCT CHARACHTERITICS,
LABELLING AND PACKAGE LEAFLET

The valid Summary of Product Characteristics, labelling and package leaflet are the final versions achieved during the Coordination group procedure.