NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 20 OF REGULATION (EC) 726/2004
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This notification is a referral under Article 20 of Regulation (EC) 726/2004 to the CHMP made by the European Commission:

Product Name(s)	InductOs
Active Substance(s)	dibotermin alfa
Pharmaceutical form(s)	All
Strength(s)	All
Route of administration(s)	All
Marketing Authorisation Holder(s)	Medtronic BioPharma B.V. Earl Bakkenstraat 10 6422 PJ Heerlen The Netherlands

InductOs is a kit for implant, authorised centrally since 2002 for single level lumbar interbody spine fusion as a substitute for autogenous bone graft in adults with degenerative disc disease who have had at least 6 months of non operative treatment for this condition. Inductos is also indicated for the treatment of acute tibia fractures in adults, as an adjunct to standard care using open fracture reduction and intramedullary unreamed nail fixation.

The kit consists of a powder containing the active substance, dibotermin alfa, a solvent and a matrix (absorbable collagen sponge, ACS). This has to be applied to the sponge which is thereafter implanted into patients. ACS has been classified as an excipient of InductOs. As such it is consequently inspected against EU-GMP guidelines.

The manufacturer of ACS, Integra LifeSciences Corporation (ILS), located in the third country (i.e. US), was inspected last in April 2015 by the Netherlands and Spain and found to be not compliant with the legal requirements and/or the principles and guidelines of GMP as provided for by Union law. The main concern identified was potential for particulate contamination.

During the previous inspection (January 2014) a number of major deficiencies were already identified. It was decided that a re-inspection would be done after one year to assess the progress in eliminating the major deficiencies. At that time, following a corrective action plan, restricted GMP certificate was issued valid until January 2015. As mentioned above, the April 2015 inspection found that the corrective action plan failed and the contamination of ACS with particulate matter was not under control and quality system not aiming for continuous improvement.

Consequently, the Netherlands issued a draft statement of non-compliance beginning of July 2015 and informed the CHMP and the Commission by a letter dated 20 July 2015.

The final statement of non-compliance was issued and entered in the Community database by the Netherlands (IGZ) in accordance with Article 111 (7) of Directive 2001/83/EC on 23 July 2015.

In view of the above, the European Commission (EC) initiates a procedure under Article 20 of Regulation (EC) No 726/2004 and requests the Agency to assess the above concerns and their impact on the benefit risk balance for the centrally authorised medicinal product InductOs. The EC requests the Agency to give its opinion as soon as possible, and at the latest by the end of the 2015 on whether the marketing authorisation for this product should be maintained, varied, suspended or revoked.

The CHMP is asked to consider if there is a need to take provisional measures to be applied immediately, notably a withdrawal of medicinal products (or certain batches thereof) from the market and/or a suspension of the marketing authorisation.

[redacted]
Sabine Jülicher
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European Commission
DG Health and Food Safety
Unit D5 - Medicinal products - authorisations, European Medicines Agency