European Commission
DG Health and Consumers
Unit SANCO/D/3 – Pharmaceuticals

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European Association of Euro-Pharmaceutical Companies

Brussels, 11 Nov 2011

PCIM/11/01 – Public consultation
on implementing measures for pharmacovigilance

Dear Ms. Brunko,

The EAEPC is the European voice for parallel distribution of medicines in the EEA area of Europe. Membership comprises around 70 mostly privately held companies from 20 countries, representing leading parallel importers that cover their respective markets between 50% (Germany), 65%(UK) and nearly 100% (France, Ireland, Italy, Denmark, Sweden, Finland, Poland, Latvia, Spain and the Czech Republic).

Parallel import (PI) is regulated by national authorities and by the EMA; in the latter context we speak about parallel distribution, whereas in the context of non-centrally approved medicines the terminology of "parallel import" is prevalent. Marketing of a centrally approved medicine by parallel distributors is subject to a parallel distribution notice issued by EMA; placing on the market of non-centrally approved medicines requires prior approval by the national regulator, and separate MAs will be issued for each dosage form and strength of a drug and for each country of source. The Commission has issued a communication in 2003 on “on parallel imports of proprietary medicinal products for which marketing authorisations have already been granted”; COM (2003) 839 final.

Parallel distributors who operate a repackaging facility must further be in possession of a manufacturing authorisation and are subject to GMP rules and inspections.

According to the communication cited above, PI authorizations issued by national authorities must be considered a marketing authorization, albeit obtained in an abbreviated procedure, as no pharmaceutical product may be placed on the market without a marketing authorisation. In this respect, and insofar as pharmacovigilance obligations are tied to a MA (marketing authorisation), parallel importers are in principle subject to pharmacovigilance responsibilities as strengthened in the recent review of the Directive.

However, that responsibility should be adapted to what parallel importers/distributors actually do to a medicine.

PI are authorised only – and instructed - to amend the packaging to adapt it to the labelling requirements of the market of importation for the particular medicine concerned. Immediate packaging is as a rule not opened and thus the medication per se is not affected. Thus there is no change to the therapeutic effect of the product and the responsibility for pharmacovigilance should remain with the manufacturer (i.e. the originator company). Parallel importers will never have access to the clinical dossier of a medicine that was filed by the manufacturer to obtain the initial MA.

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In the circumstances of the EMA Parallel Distribution notification scheme, the agency is totally responsible for the product file, and one sole MA is applying to all 27 Member States. Here the importer is acting only as a distributor, and should be exempted from all product-related pharmacovigilance considerations.

As regards national PI licence grants, pharmacovigilance responsibilities should only pass to the importer in very restricted circumstances such as (but not limited to) the following:

- the imported and national product does not share a common origin;
- the imported product contains different excipients to the national product;
- the imported product contains an active ingredient made by a different route than that used in the national product;
- the imported product is a sterile product, sterilised in a different way from the national product;
- bioequivalence of the imported and national product cannot be demonstrated through bioavailability studies.

By way of example I refer to the guidance on the "pharmacovigilance system for parallel imported products" which the UK MHRA has issued (http://www.mhra.gov.uk /home/groups/l-plpi2/documents/websiteresources/con057402.pdf).

In the submission on "Safe medicines in parallel trade" to your directorate on 30 March 2007, we had indicated the pharmacovigilance practice of parallel importers, consisting of reporting ADRs and defective products:

ADR reporting: ADR reports by patients, doctors or pharmacists, that concern parallel imported products, may be directed to the importer or often directly to the regulator. If a parallel importer/distributor receives an ADR, he will reply directly to the complainant, keeping full documentation of the ADR. If the ADR is of a serious nature, the parallel importer will then inform the authority, and in case of repeated ADRs on the same products also the manufacturer. This is particularly the case if the complaint reveals a deviation from the information contained in the PIL.

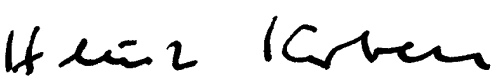
Quality defect reporting: Parallel importers or distributors who repack or re-label products are obliged to open each pack, thereby carrying out an optical inspection of the medicines unpacked. This operation has commonly revealed a number of quality defects of incoming goods, which routinely leads to the elimination of the entire pack from the supply chain. There is no systematic filing of such incidents by parallel importers, but in cases of severe or repeated defects, manufacturers will be informed.

In conclusion, the Commission may envisage to refer to the UK regulation as a suitable standard for the pharmacovigilance system of parallel imported products that could be applied by our sector also in other member states in the absence of specific guidance issued nationally.

Thank you for the opportunity to make these belated comments.

Kind regards,

Heinz Kobelt



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