IPEC EUROPE APPROACH TO THE LACK OF A MASTER FILE SYSTEM FOR EXCIPIENTS IN EUROPE

Over several years IPEC Europe has addressed the European authorities on a number of occasions regarding the need for an excipient master file (EMF) system in the European Union. In these discussions **IPEC Europe has proposed that the current EU Active Substance Master File (ASMF) system should be extended to encompass excipients, and mainly for novel excipients**.

We strongly believe that an EMF system is needed in Europe to:

- Allow novel/specialised excipient developers and manufacturers to **protect their confidential information** by submitting it directly to the EU regulatory authorities, and **enable direct communication between the assessors and the excipient experts**.

- **Reduce the bureaucratic burden on the EU** by removing the need for extensive information to be included in numerous drug dossiers, thus avoiding multiple assessments and duplication of review efforts by the authorities.

- **Remove the commercial and administrative disadvantage that novel excipient developers face in Europe in comparison to other regions of the world** (e.g. USA, Japan, Australia, New Zealand, and Canada) by providing a workable regulatory system for the introduction of their products. This would reduce the burden on excipient manufacturers (often Small and Medium Enterprises) and end users alike and in turn facilitate the development of new and/or improved medicinal products.

- **Enable a standardised approach to the submission of excipient information to the authorities**, not just throughout Europe, but worldwide.

- **Provide the flexibility necessary to accommodate the broad range of new therapies and technologies** rapidly emerging onto the EU and global market.

Specifically IPEC Europe is advocating the use of a partially closed master file system for excipients as is currently used for ASMFs. This would be a **voluntary approach** for the excipient manufacturer allowing him to protect his confidential information within the Closed part of the master file. The user/MAH (Marketing Authorisation Holder) would have access to all the information needed to take full responsibility for its intended use in their drug product in the Open part of the EMF.

IPEC Europe considers that an EMF would only be required **for defined cases**. In practice this is likely to apply mainly to novel excipients, i.e. those referred to in the EU Notice to

Applicants Volume 2B[1] – paragraph 3.2.P.4.6 - as: "*[…] excipient(s) used for the first time in a drug product or by a new route of administration […]*", and in general would not be necessary for compendial excipients.

The EU authorities could identify categories of materials that they would consider appropriate for EMF submission in a similar way to both the US and Japanese systems. The FDA have specified four types of Drug Master File (DMF) for pharmaceutical components including Type IV DMFs for excipients[2], while the MHLW have also stated which items can use their DMF system including new and mixed excipients[3].

In conclusion, IPEC Europe believes that improving the functionality of the EU master file system is a fundamental part to control the impact of excipient quality and safety on drug products and ultimately to facilitate faster access of European consumers to novel and safe therapies. Furthermore, extending the master file system to excipients would be an **appropriate measure to be in line with the European Commission's intention[4] to improve EU regulatory environment** to encourage innovation and increase competitiveness in the pharmaceutical area.

The European Commission has already acknowledged the need to further reflect on the ASMF concept, with a view to extending its scope, in particular with respect to efforts towards the international harmonisation of regulatory frameworks, most notably between the US, Japan and the EU. However, currently the EU system remains more restricted than in those and other regions of the world, being not open to excipients.

Thus, given the lack of such a system so far and until further progress is made in the EU, IPEC Europe proposes the following approach for its member companies when responding to requests from the MAH to provide confidential data which are not fundamental for the safety and quality of the medicinal product:

- **State that the specific requested information is available but confidential, and**
- **Stress that, as excipient manufacturer, your company would be glad to supply the information directly to the European authorities.**

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1 See: http://ec.europa.eu/enterprise/sectors/pharmaceuticals/files/eudralex/vol-2/b/update_200805/ctd_05-2008_en.pdf
2 CDER Guideline on Drug Master Files (DMF), September 1989 as amended. See: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073164.htm
3 MHLW yakushoku shinsa-hatsu No.0210004. See: http://www.pmda.go.jp/english/service/pdf/notifications/Guideline_on_Utilization_of_Master_File_for_Drug_Substances,_etc.pdf
4 See better regulation initiative: http://ec.europa.eu/governance/better_regulation/index_en.htm