

IPEC Europe Position Paper on the Proposal for a Directive on Falsified Medicinal Products

22 January 2010

Executive summary

IPEC Europe¹ welcomes the “Commission proposal for a Directive of the European Parliament and of the Council amending Directive 2001/83/EC with regard to the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source” and agrees that action is required to protect all European citizens from the resulting unsafe medicines.

Currently some Members of the European Parliament and some delegations of the Council of the European Union have suggested in their draft amendments **to extend the scope of this Directive to encompass excipients**.

IPEC Europe strongly believes that, if excipients are indeed to be included within the scope of the proposed directive, the EU Regulators currently addressing the matter on counterfeit excipients should consider the following recommendations:

- **A more accurate definition of “excipients” than the one currently proposed in the draft amendments should be used in this Directive. IPEC Europe would like to suggest the following definition: “*Pharmaceutical excipients are substances other than the Active Pharmaceutical Ingredient (API) which have been appropriately evaluated for safety and are intentionally included in a drug delivery system.*”**
- **The differences between pharmaceutical excipients and APIs should be reflected throughout the directive, acknowledging in particular that different GMP and GDP than those of APIs should apply to excipients.**
- **The GMP and GDP for excipients used in medicinal products should be defined in a separate section of the EU rules. An excipient drug master file (DMF) system for data protection should also be created.**
- **GMP and GDP requirements for excipients should not be more demanding on the industry than the current widely-accepted IPEC-PQG GMP and IPEC GDP Guides.**
- **Third parties audits and GMP/GDP inspection certifications by national authorities should be kept on voluntary basis or “for cause” to allow the management of resources by both industry and Member States as appropriate.**
- **Keep a balanced approach to enhance patient safety while ensuring the maintenance of a thriving excipient industry in Europe.**

Clarification of key points

The report of the impact assessment² for a Directive for a list of certain excipients³ concluded that compared to current policies a **Commission Directive on GMP for excipients was not expected to lead to benefits to patients but to increased costs**. Thus, in June 2009 DG Enterprise and Industry concluded that “a balanced approach for requiring GMP for excipients within the concept of legal requirements on manufacturing and quality control in the legal pharmaceutical framework” should be used. The current draft amendments do not acknowledge these findings.

¹ IPEC Europe, the International Pharmaceutical Excipients Council Europe, is an association that serves the interests of producers, distributors and users of pharmaceutical excipients; it represents approximately 80 member companies in Europe.

² http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_02/excip_report_20071219.pdf

³ Pursuant to Article 46(f) of Directive 2001/83/EC as amended.



IPEC Europe acknowledges that if APIs can be counterfeited, then so can excipients. **But excipients are completely different to APIs when used as starting material. In the majority of cases they are not intended or designed specifically for such applications, being manufactured and sold to a broad spectrum of industry users.** These consist of well known ingredients often consumed by citizens in many different products – for example sugars like sucrose or lactose, cellulose, talc, citric acid, gelatine, mint flavouring – which are well regulated and controlled also by other pieces of legislation and practices. Thus any legislation impacting excipients' manufacture and supply requires very careful consideration if ultimately pharmaceutical products are to remain available in the market, and at a reasonable cost for European patients and healthcare systems.

Should the corresponding standards for APIs be applied to excipients then the impact on the pharmaceutical industry would be very detrimental. The cost of implementing API standards for excipients would often be many times the annual sales revenue of the excipient resulting in withdrawal of excipients from the market, making such a proposal not enforceable and not applicable. As excipients are not always manufactured with the intention of being used for medicinal products, **any identification of imports or exports of excipients is going to be very difficult.** Many other legitimate uses for these materials could be caught up in the implementation of this Directive, thereby having a serious impact over a much wider part of the economy than merely pharmaceuticals.

In addition, counterfeiting is more favourable when conditions of a very high level of demand exceed the legitimate supply. Applying APIs standards would make it more attractive to produce excipients outside the EU, especially in low cost manufacturing regions of the world creating an **increased opportunity for criminals to exploit excipients.**

IPEC Europe defines pharmaceutical excipients as **“substances other than the API which have been appropriately evaluated for safety and are intentionally included in a drug delivery system.”** This underlines the important aspect that the excipient has been appropriately evaluated for safety in relation to the direct exposure to patients. The definition in the draft amendments overlooked this critical aspect of safety evaluation of excipients which is vital to meeting the needs of industry, patients and healthcare systems.

The Draft directive also proposes using third parties to ensure that excipients have been made to GMP and distributed to GDP, and its development is welcomed. **IPEC and its partners⁴ are developing a suitable third party audit scheme for marketing authorization holders to be used in exactly this manner.** The GMP and GDP will be as currently defined in the well worldwide received and implemented IPEC-PQG GMP and IPEC GDP Guides⁵. In fact IPEC Europe as a responsible industry body is engaged since its creation with other international partners to develop voluntary international accepted standards and best practices.

It is desirable that excipient manufacturers throughout Europe should be able to **obtain GMP Certificates from their national inspection authorities on a voluntary basis** (currently this is only available in some member states). Such certificates will aid European exports to destinations which routinely require GMP certificates. Mandatory GMP certificates for excipients would create administrative bottlenecks. Furthermore the national inspectorates are already finding it difficult to complete all the inspections required for drug products and APIs. Including excipients into their scope will require a significant resource increase if the other duties are not to suffer. **The EU is also still lacking a master file system for excipients**, which is in place in many regions of the world (e.g. USA, Japan, Australia, New Zealand, and Canada). To apply appropriately GMP, GDP, site registration and inspections there should be facility for Drug Master Files (DMFs) for excipients.

In conclusion the details and principles in the Directive are to be welcomed in that they will enhance patient safety. However a balance has to be struck between the burden of implementation and the need to ensure a viable and thriving European excipient industry. Overall IPEC Europe believes that the proposed Directive should establish a level playing field for the excipient industry in the community.

4 EFCG, FECC, PQG, and IPEC Americas.

5 See IPEC Europe website at: <http://www.ipec-europe.org/page.asp?pid=59>