9 April 2012

Unit SANCO/D/6
DM24/028
BE-1049 Brussels
BELGIUM

By Email:
sanco-pharmaceuticals-d6@ec.europa.eu

RE: Comments on the European Commission's Concept Paper Submitted for Public Consultation *"Delegated Act on the Principles and Guidelines of Good Manufacturing Practice for Active Substances in Medicinal Products for Human Use"* Sanco.ddg1.d.6(2012)73176.

Dear Sir or Madam:

The Bulk Pharmaceuticals Task Force (BPTF) of the Society of Chemical Manufacturers and Affiliates (SOCMA) appreciates the opportunity to provide comments on the concept paper submitted for public consultation "Delegated Act on the Principles and Guidelines of Good Manufacturing Practice for Active Substances in Medicinal Products for Human Use."

About BPTF

By way of background, the BPTF, an affiliate of SOCMA, is an association for manufacturers of active pharmaceutical ingredients, excipients and intermediates. Our primary objective is to seek clarification of the current regulatory requirements for our products and to interact with governmental agencies on emerging issues that may impact SOCMA members. SOCMA is the leading US trade association of the specialty batch and custom manufacturing chemical industry representing approximately 300 member companies with more than 2,000 manufacturing sites and over 100,000 employees.

As global suppliers of active drug substances and excipients, BPTF members support the European Commission's Health and Consumers Directorate initiatives to secure the supply chain and protect the access to quality drug products for all Europeans.

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Comments on The Concept Paper

The concept paper "Delegated Act on the Principles and Guidelines of Good Manufacturing Practice for Active Substances in Medicinal Products for Human Use" explains that its goals are to facilitate the implementation Directive 2011/62/EU. This directive's purpose is implied in its title: "the prevention of the entry into the legal supply chain of falsified medicinal products."

We call your attention to Line 9 and 10 of concept paper, which reads as follows:

> *Against this background it is therefore currently envisaged to extend the scope of Directive 2003/94/EC to active substances. Consequently, subject to certain modifications (see below), the provisions of Directive 2003/94/EC would also apply to the manufacturing of active substances.*
>
> *This approach would bring coherence:*
> - *in terms of the regulatory setting (Commission Directive plus detailed Commission guidelines) for both medicinal products and active substances; and*
> - *in terms of substance: the principles and guidelines for GMP would be the same during the manufacturing of active substances as well as medicinal products.*
>
> *Moreover, this approach would allow relatively swift adoption of GMP for active substances, thus giving legal clarity to Member States and stakeholders.*

As per Consultation Item No. 1, the BPTF does not agree with this appraisal nor approach to extend a modified EudraLex - Volume 4, Part I to APIs.

- Falsified Medicines. Extending drug product GMPs to APIs does not prevent falsification. In fact, it raises the incentives for those engaged in this illegal activity. Falsification allows unscrupulous manufacturers to avoid the higher costs of compliance, yet sell aggressively in a higher cost market.

- ICH Q7. "Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients" ICH Q7 was issued as harmonized tripartite guideline to bring *coherence*[1] of approaches to GMPs for APIs across the key manufacturing jurisdictions. Contrary to this, modifying the provisions of EudraLex - Volume 4,

[1] International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, CONCEPT PAPER: Q7 – Good Manufacturing Practices for Pharmaceutical Ingredients (5 February 1998) http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/ Quality/Q7Concept_papers/Q7_Concept_Paper.pdf

Part I, as proposed in the Concept Paper, presents a disharmonization. This will lead to confusion across the tripartite regions and across the world-wide supply chain.

ICH Q7 recognizes explicitly that the processes, facilities, and quality challenges faced by API manufacturers using chemical, fermentation and/or isolation techniques are unique. The principles of ICH Q7 align with Directive 2003/94/EC, but there are substantive differences. ICH Q7 has served the pharmaceutical industry and European public well. The Concept Paper fails to identify any shortcoming of this quality standard, nor explain why it should be abandoned.

Unintended Consequences

The generic API industry is highly price competitive. The cost of the modifications required to bring existing API facilities into compliance with this different standard EudraLex - Volume 4, Part I may force some API producers to choose to exit the European market. The implementation of drug product GMPs for APIs will further accelerate the relocation of API manufacturing to low-wage, third-world jurisdictions, where the costs of these increased and inappropriate requirements would be better borne. The supply chain, if anything, would be less secure in these countries, which are known to have poor regulatory oversight and which are the source of many of the falsified medicines. Additionally, with fewer qualified suppliers, European countries could begin to experience drug shortages similar to those seen in the United States. In short, the security of supply of APIs in Europe could be jeopardized by this unwarranted rule making.

We appreciate your consideration of these comments. The BPTF is committed to providing our customers quality APIs and excipients under robust quality systems for the production of safe and effective drugs for all Europeans.

Sincerely,

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