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Sent: Wednesday, November 28, 2012 6:33 PM
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Subject: HLWG; regulatory issues; pharmaceuticals ; meeting with EFPIA on 26 Nov; report

General points:

- **Very productive** meeting with EFPIA and their regulatory expert (present Sanco, ENTR and TRADE). EFPIA was updated on the process in the HLWG. We indicated that their industry would be among those to present their proposals at the next HLRCF meeting. EFPIA and PHRMA's joint submission is very well structured and a good basis for further discussions.
- **EFPIA members remain committed** to the process while flagging "issue"-fatigue sometimes encountered in their discussions with FDA and EMA stemming from earlier and fruitless initiatives to make our regulatory approaches more coherent.
- For the EU side, EFPIA flagged that for some of the initiatives proposed in the joint paper, **cooperation from Member States would be required** (for example in the case of mutual recognition of inspections assessing compliance with GMP or GCP).
- Interestingly, and similar to submissions from BRT and TABD, **EFPIA also calls for the establishment of a "high level standing group"** with a political mandate to also work on new regulatory issues, which may arise during and after the negotiations in the area of pharmaceuticals.

- As a next step **EFPIA and PHRMA will provide more details on their proposals**, especially the more short-term ones, outlining the main objectives and outcomes for a possible FTA bearing in mind timing and feasibility. EFPIA will come back to us still before the end of the year.
- **EFPIA will also submit a paper elaborating on additional issues** not contained in the joint paper. *NB: As regards the submission by EGA-GPhA, EFPIA can support all the points made although views somehow differ obviously as to advanced manufacturing.*

The following specific points were made by EFPIA:

- EFPIA proposes EZU and US should mutually recognise inspection findings for both GMP and GCP inspections: Proposal is to push for MR, based on the already existing good collaboration this goal could be achieved in the short- to medium term. There is good cooperation and PIC/S scheme based on European standards, but MR has not been achieved so far, due to concerns regarding liability. But these could be overcome, as the US has also concluded ME agreements with other jurisdictions. Another complicating factor was difference in MS practices as to inspections. At present, the industry is sometimes faced with multiple inspections (i.e. one site got visited 20 times in a row). This is inefficient and raises compliance costs, for both industry and the administration.

- Parallel Scientific advise: Proposal is for EU and US companies to have joint sessions with regulators when they request scientific advise, after clinical trials have been carried out, on the basis of a joint list of questions – this would also allow to reconcile the feed-back received. This could be short- to medium term achievement. To date, companies need to have separate discussions with FDA and EMA and questions and evaluations vary, with negative consequences on the predictability for industry. Similar objectives are sought for Quality by Design (QbD) applications. EFPIA and PHRMA will provide further details how to achieve this aim in practice.

- Pediatric medicines: Proposal is to streamline the process and allow companies to prepare one and the same pediatric plan in EU and US. Industry faces problems due to the "great differences" in the approach by FDA and EMA, stemming mainly from interpretation (by the ECJ) and application of the ICH guidelines in particular the rules on the design of studies, leading sometimes to the duplication of tests and delays which are costly for the companies concerned. Sanco is preparing a report on the respective EU Regulation. In general industry considers the EU approach too burdensome (as compared to the US approach) as it requires companies to generate data for the condition rather than the specific indications within that condition – this leads to more studies. Difference in timing is also an issue.

- Safety Reporting requirements: Proposal is that FDA and EMA should expand and strengthen their cooperation on "pharma-covigilance". Again, EU and US interpret ICH guidelines differently; problem is also that in the EU there are only a few centrally approved medicines, and a lot is done at MS level.

- Duplicative clinical testing: Proposal is to work in ICH to revise ICH guidance to make easier the use of foreign clinical trial data (and approval by agencies). At present, both FDA and EMA can require additional studies before giving approval and this is costly for the companies concerned. More medium- to long-term.

- Benefit-risk assessment: Proposal is to harmonise the assessment for drug review and approval. This is a more long-term goal. EFPIA and PHRMA will provide more information.

- Submissions on manufacturing changes: Proposal is to harmonise approach to post-approval variation submissions. I.e. what changes are major, what changes moderate or minor- since this would require change of legislation it is a more long-term objective.

- Other items: Disclosure of clinical trials (which data the EU and US agencies publish on clinical trial results – this is related to IPR). Collaboration on scientific and other guidance on therapeutic areas (more information needed as proposal is vague); Falsified medicines: this proposal is related to the development of common standards to encode medicinal products and verify their authenticity.