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Project Acronym: CCRYSTAL

Project Full Name: Innovative equipment and methodologies for
APIs continuous crystallization

Final Report

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Final Report

PROJECT FINAL REPORT

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Project acronym:	CCRYSTAL
Project title:	Innovative equipment and methodologies for APIs continuous crystallization
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Final Report

Please note that the contents of the Final Report can be found in the attachment.

4.1 Final publishable summary report

Executive Summary

The expiry of patents for major blockbuster drugs and the entry of low-priced generic versions are expected to increase the consumption of generic drugs, with the weak pipelines of major pharmaceutical companies amplifying this trend. With many patent expiries occurring during 2010-2012, generic consumption is expected to peak, and in turn increase the competition between pharmaceutical producers.

The global pharma players are looking at sourcing cheaper APIs, particularly in the situation of weak purchasing power worldwide. This is because of patent expiry of the blockbuster drugs, cut in medical costs in developed world and rise in R&D spending. Therefore, the opportunity descends upon low cost producers such as Chinese API makers. The Project aimed at introducing advanced technologies to complete continuous manufacturing processes of pharmaceutical substances with enhanced, mainly continuous, crystallization technologies, affording fundamental new approaches to obtain products with high purity levels and constant and reproducible crystalline forms at a competitive price, enabling EU APIs industry to regain his competitiveness against Asian Producers. The innovative technologies, jointly with the new processes for 4 selected APIs developed during the two year of the Project lifetime, are based on a new concept crystallizer and on continuous mode operation. From the point of view of drug manufacturing economic analysis, the new technologies are especially important for the market of generic APIs. Generics are changing the companies' strategies. The incidence of drug substance manufacturing cost on the price of the final pharmaceutical specialty was really not relevant for under patent drugs. This generated small or no attention to API manufacturing cost reduction and, as a consequence, process improvements. Now generic companies are experiencing more and more competition, and their business logics are resembling those of fine chemical producers. So they have to improve their processes in order to remove the more relevant inefficiencies that are related to organizational aspects as well as to raw material costs reduction. As an example, for what the batch/continuous process comparison is considered, batch processes need to "STOP" because of repeated sampling and isolation at every intermediate step. Such a situation will force companies to innovate and move from "quality by analysis" to "quality by design" manufacturing. To reach this goal a complete command of the process has to be reached in order to avoid being victims of "analysis paralysis". To get out of this situation; alternate manufacturing scenarios are under consideration. Contract manufacturing organizations (CMO) specialize in certain chemistries, unit processes, and operations and campaign their production. Based on the amount of API needed, some of the products are campaigned in pilot plants to mini-plants. Modular plants are going to be an excellent option for batch or continuous processes. Innovation in manufacturing methods, improved process technologies, along with good manufacturing methods deliver excellent processes and are able to handle low to high production rates. Better manufacturing technologies for API and formulation are expected to improve profits at that level. For API, the improvements come in the way of improved yield, reduced waste, reduced and better solvent use, improved productivity, and improved business processes. For formulations they come with the blending, size uniformity and uniform admixing, etc. In the supply chain there are opportunities and one has to pick them. Improved technologies will also significantly reduce their carbon footprint. Companies that are excellent in manufacturing API and formulating drugs are now acting as the innovation driver more than the companies dedicated to invent new active principles.

Summary description of project context and objectives

The CCRYSTAL fits into a context of continuous changes in the market it refers to, namely that of APIs.

The following trends were registered during the last two years:

- # Evolution of API regulatory requirements;
- # Expansion of the use of continuous technologies in API production processes;
- # Increase of technological level of Companies producing in emerging Countries;