



Project number: **LSH-2002-1.2.5-2**

Project acronym: **PHARMA-PLANTA**

Project title: **RECOMBINANT PHARMACEUTICALS FROM PLANTS FOR HUMAN HEALTH**

Instrument: Integrated Project

Thematic Priority: Life Sciences 1

# **THIRD PERIODIC ACTIVITY REPORT OF THE PHARMA-PLANTA CONSORTIUM Publishable Executive Summary**

Covering period from 1<sup>st</sup> February 2006 to 31<sup>st</sup> January 2007

Project start date 1<sup>st</sup> February 2004

Project coordinator: Fraunhofer Gesellschaft

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## **PUBLISHABLE EXECUTIVE SUMMARY**



Pharma-Planta is an EU Sixth Framework Integrated Project whose primary goal is to develop an approved production pipeline for plant-derived pharmaceutical proteins (PDPs). Although previous research has developed proof of the PDP concept, Pharma-Planta aims to develop an entire production chain by taking candidate pharmaceutical molecules from the expression platform through all stages of production and processing, ultimately to initiate phase I human trials in Europe. At the end of its third year, the Pharma-Planta Consortium comprises more than 40 interacting groups including public institutes, SMEs and larger industrial collaborators from 11 European Member States and South Africa.

The objectives of the program can be summarized as follows:

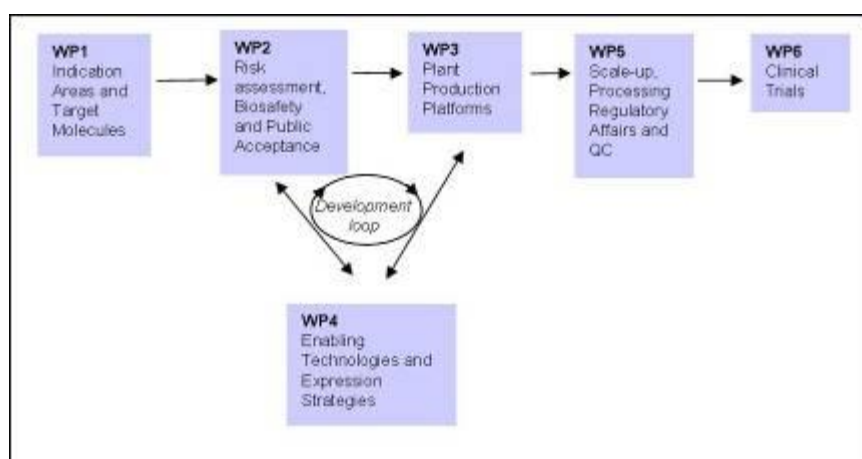
- To produce recombinant pharmaceutical molecules in transgenic plants. These will be developed through all regulatory requirements, GMP standards and pre-clinical toxicity testing and will be evaluated in Phase I human clinical trials.
- To develop robust risk assessment practices for recombinant pharmaceutical molecules produced in plants, based on health and environmental impact, working with regulatory authorities within the EU as well as public groups to ensure that the production systems are as safe and as acceptable as possible, and that they comply with all biosafety regulations.
- To define and carry out a coordinated program for securing and managing intellectual property that will facilitate the availability of high priority plant-derived recombinant pharmaceuticals to the poor in developing countries while simultaneously allowing the products to be developed commercially in Europe and North America.
- To develop and refine new strategies for the expression of recombinant pharmaceuticals in plants, which can be used on a generic basis for molecules that are normally expressed poorly.

- To develop and generate transgenic plants expressing a second generation of recombinant molecules that will be used in future clinical trials.

At the beginning of the project, eight target molecules were chosen representing four key indication areas – HIV, tuberculosis (TB), rabies and diabetes. These molecules comprised two HIV antibodies, two HIV antigens, two rabies antibodies, a TB antigen and a diabetes autoantigen. Early in the first project year, the two HIV antibodies were selected for fast-track production, meaning that these molecules were to be taken through the production pipeline as pioneers, progressing through the key areas of risk assessment, plant production, scale-up and regulatory development, with the aim of submitting at least one of them for clinical trials within the five years of the program. In the third year, an additional HIV antibody was added to the fast-track program, bringing the total number of target molecules to nine. As well as the fast-track, there is also a ‘development loop’ of enabling technologies to improve product yield and quality.

The project is divided into six interacting work packages, as shown in **Figure 1.1**. WP1 provides the target molecules and the assays for their detection in transgenic plant material, so by the end of year 3 most work in WP1 was complete. WP2 considers the potential environmental impact of different strategies for PDP production, and leads interactions with appropriate regulatory agencies and other stakeholders. The role of WP2 has intensified this year, due to increased contact with EFSA and EMEA and due to the development of dossiers for risk assessment and standard operating procedures. WP2 has also taken on the responsibility for preparing the clinical trials dossier in collaboration with WP6. WP3 provides expression platforms for the fast-track molecules and generates the bulk material for their production. This year has seen intense work from the WP3 maize and tobacco groups, including the selection of plant lines expressing high levels of the recombinant antibodies, resulting in the project’s first batches of production grade material. WP3 also includes a cluster of groups working on plastid expression, and this year saw the successful expression of HIV antigens in tobacco chloroplasts with advances also made in tomato and lettuce plastid transformation. WP4 is the development loop, which includes a diverse range of expression platforms and technologies for improving protein yields. Most of the work initially envisaged for WP4 had been completed by the end of year 3, although some of the groups involved in this WP

continue to pursue the work initiated under the Pharma-Planta programme using other sources of funding. WP5 oversees the scaling, processing, quality assurance and quality control of the fast-track material, and also leads interactions with regulatory agencies concerned with GMP in pharmaceutical production. The work carried out in WP5 has stepped up this year, first in terms of the process development for plant-derived material and second in terms of the close cooperation with WP2 in engaging the regulators and helping to develop appropriate and workable guidelines. Finally, WP6 is charged with organizing and performing the clinical trial. The groups in this WP have begun to develop and outline a clinical protocol for an HIV microbicide. They have also begun to explore the preclinical studies that will be required before any of the HIV antibodies can enter phase I trials.



**Figure 1.1**  
Organization of the  
Pharma-Planta  
programme

Pharma-Planta is coordinated by the Fraunhofer Gesellschaft, which provides professional project management, administrative and financial coordination, and IT support. Scientific aspects of the project are coordinated by Professor Julian Ma of St George's Hospital Medical School, where the clinical trials will be performed. The management of the program also includes components to carry out biosafety risk evaluation (partner 5a), management of intellectual property (handled by MIHR, partner 32) and a comprehensive training program (chaired by Paul Christou, partner 35). Two rounds of competitive applications for PhD studentships were invited in year 1 of the program, and the projects approved in these applications are now in progress. A final round of applications was invited this year and the project positions are now being filled. These studentships complement and extend the work envisaged within the Technical Annex thus giving the project added value.