Section 1. Publishable executive summary

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The main scientific and technological (S&T) objectives of HIPPOCRATES project were:

1. Development and optimization of processing techniques that allow for the production of new alternative biodegradable scaffolds from natural origin polymers and ceramics with adequate structure/properties for different tissue engineering applications.
2. Optimization of the surface characteristics of the scaffolds in order to enhance cell adhesion and proliferation and control the cell differentiation.
3. Developing of red algae culturing techniques that allow for their growth and mineralization in conditions adequate for producing suitable hydroxyapatite/tri-calcium phosphate scaffolds with tailored morphologies to be used on tissue engineering.
4. Developing adequate processing routes to produce synthesized hydroxylapatite mimicking the natural occurring morphology.
5. Using of rapid-prototyping methodologies to design and process scaffolds tailored to patient needs, and enabling for the loading of growth factors during scaffold processing.
6. Developments and optimization of a technology that allow for the combination of ceramic and polymeric structures in order to develop specific matrices for the regeneration of osteochondral defects.
7. Extensive *in-vitro* characterization of all the developed and modified materials in order to optimize their properties.
8. Comparison of the effects of different growth factors and differentiation factors on the final tissue engineered products.
9. Development of the respective ways of expressing and purifying the distinct growth factors.
10. Optimization of primary cell cultures (human osteoblasts and chondrocytes) and their seeding/performance on the developed scaffolds.
11. Obtaining an alternative source of cells for tissue engineering by means of establishing culture conditions that allow the differentiation of human progenitor cells into the osteoblastic and chondrogenic lineages.
12. Optimization of cell isolation and cell culturing techniques by means of developing original real-time monitoring methodologies.
13. Optimization of the cell culture conditions on the porous scaffolds and *in-vivo* testing of the functionality of the hybrid construct materials in adequate animal models.

No	Role*	Participant name	Short name	Partner	Team Leader	Country
1	CO	3B's Research Group, Dept. Polymer Eng., University of Minho	**3B's-UM**	1	Rui L. Reis (CO) João Mano	Portugal
2	CR	ENVISIONTEC GmbH	**ENTEC**	2	Volker Schillen	Germany
3	CR	Ludwig Boltzman Institute, Trauma Care, Vienna	**LBI**	5	Heinz Redl	Austria
4	CR	Queen's University of Belfast, Marine Laboratory	**QUB**	4	Mathew Dring	UK (N. Ireland)
5	CR	MATERIALISE NV	**MAT**	3	Jeroen Dille Bart Veeckmans Roel Wirix	Belgium
6	CR	Johannes Gutenberg University, Institute of Pathology, Mainz	**JGU**	7	C. James Kirkpatrick	Germany
7	CR	Red Cross Blood Transfusion Center of Upper Austria	**RCROSS**	6	Christian Gabriel	Austria

*CO = Coordinator , CR = Contractor

Several of the academic and industrial partners, were involved on some of the most successful and more highly funded EU biomaterials projects in FP4 and FP5 (see EU press-release on http://europe.eu.int/comm/research/growth/gcc/projects/in-action-biomat01.html) namely those that were more connected to bone and cartilage. In fact the coordinators of the **PHIDIAS** project and **ISOBONE** partners are also part of the **HIPPOCRATES**. Several of the partners were also involved in a major CRAFT programme on bone repair materials, the **ALGISORB**. All partners are involved in several projects in the FP6 in the tissue engineering field, namely the Network of Excellence (NoE) **EXPERTISSUES** which shares the same coordinator (3B's-UM).

3B's-UM, the coordinator, has been working, having joint publications, projects and student exchanges with many of the involved partners and was deeply involved on two of the above cited projects. There was also already a strong cooperation between several of the **HIPPOCRATES** partners. The companies of the partnership cannot develop alone one complete product able to be competitive in the international market. Being part of **HIPPOCRATES**, they were working together, with other companies and their academic partners, for the development of products, technologies and therapeutic procedures. The companies in the **HIPPOCRATES** consortium were not competitive between them but were complementary to each other. The aim was to develop the knowledge and intellectual property required to introduce new products for the proposed applications in clinical applications. This was achieved by means of applying several options (raw materials, processing technologies, growth factors, release systems, surface modifications, culturing technologies and bioreactors, etc.) and each company aimed at developing new products that are intermediate steps on the way to the final product/therapy.

Regarding the industrial partners, **ENTEC** is a tissue engineering and rapid prototyping (RP) company that has patented the 3D-*Bioplotter* System that uses a computer-aided plot procedure with a tri-axial dosage system, being designed for use in tissue engineering. It enables generation of three-dimensional cell scaffolds from a variety of biomaterials for tissue engineering and the construction of patient-specific scaffolds and drug delivery systems. It is the first system capable of processing hydrogels for the creation of soft tissue and hard polymers for the creation of bone substitute and also of integrating living cells. It works in a well-established collaboration with **MAT**. This company was founded in 1990 as a spin-off from the University of Leuven and is well known for leading the FP5 PHIDIAS project. Today it is a private company with several fully owned subsidiaries in Europe, Asia and the USA. **MAT** develops software that facilitates the use of Rapid Prototyping machines, namely the "MIMICS" software. **MAT** had appropriate expertise to project custom scaffolds based on medical images and benefited with new upgrades of the existing softwares more focus on tissue engineering applications.

The consortium also incorporated **RCROSS** that was in a unique position to obtain and multiply human progenitor and human stem cells. **LBI** is well known for its works on wound and bone healing and the use of adequate animal models to test biomaterials and tissue engineering scaffolds. Another of the roles of **LBI** in this project was to produce several growth factors, and further testing of the effect of BMPs *in vivo*. **JGU** is a recognized group of excellence in a range

of cellular biology fields and has contributed to study the biocompatibility with relevant human cells of new developed systems. More complex *in vitro* systems were developed, for example, three-dimensional cultures, cultures in dynamic conditions as well as co-cultures of different types of cells to simulate the *in vivo* situation in bone/cartilage tissue engineering. **QUB** has a strong international reputation for working on the photophysiology of marine algae. Their main contribution for this project was the algae growth for the production of calcium phosphate scaffolds from algae origin.

Finally, the **3B's-UM** has a long experience in the development of scaffolds from natural origin biodegradable polymers using a wide range of non-conventional processing methodologies, such as melt based technologies, micro-wave baking and expansion, etc. It is also involved in development of new biodegradable materials and controlled release strategies. This partner already co-operates with most of the partners involved in the project, has a strong history of cooperation with the biomedical industry, being well known internationally in the field of tissue engineering for its unique interdisciplinary research approach. Finally, it has great experience in EU funded research and was the co-ordinator of the **HIPPOCRATES**. The following scheme aims to overview the workflow of the project.