Executive summary:

4.1.1 Executive summary:

Traditional Chinese medicine (TCM), especially Chinese herbal medicine (CHM) and acupuncture, is the ancient medical system used by the people in China and some other Asian countries for thousands of years to maintain the health of one of the largest populations in the world [1,2]. In recent years, TCM has been used by an increasing number of people in Europe and has attracted intense research interests from European scientists [3,4,5].

As an emerging area in Europe, TCM research requires collaboration and coordination. Good Practice in Traditional Chinese Medicine Research in the Post-genomic Era, also known as GP-TCM, was the 1st EU-funded Seventh Framework Programme (FP7) Coordination Action dedicated to informing the best practice and harmonising TCM research through interdisciplinary exchanges among TCM experts and scientists [3].

The project studied the state of the art of TCM research, especially focusing on those most relevant to the health of EU citizens. With its large pool of expertise across 24 countries including 15 EU member states, the consortium provided fora and collaboration platforms on quality control, extraction technology and component analysis, toxicology, pharmacology and regulatory issues of CHM, and also on acupuncture studies, with a particular emphasis on the utilisation of a functional genomics approach, i.e. by addressing whole profiles of DNA, RNA, proteins, metabolites and biological activities through comprehensive bioinformatics analysis.

With its 3.5-year programme and 10 interactive work packages (WPs), the GP-TCM consortium made great efforts to identify the state of the art in the various aspects of TCM research, to develop guidelines and to agree on priorities, challenges and opportunities, as summarised in the open-access GP-TCM Journal of Ethnopharmacology special issue (see http://www.sciencedirect.com/science/journal/03788741/140 online) [6]. Based on polls of opinions among consortium members and non-members, high-quality efficacy/effectiveness, safety and mechanistic studies were identified as grand priorities and that the TCM legacy in general and its management of chronic diseases in particular were regarded grand opportunities. Consortium members cast their votes of confidence in omic and systems biology approaches to TCM research and believed that quality and pharmacovigilance of TCM products are not only grand priorities, but also grand challenges. Non-members, however, gave priority to integrative medicine, concerned on the impact of regulation of TCM practitioners and emphasised intersectoral collaborations in funding TCM research.

To ensure sustainable EU-China collaboration in TCM research beyond the lifespan of GP-TCM (May 2009 - October 2012), the Seventh Framework Programme (FP7) consortium led the establishment of a new not-for-profit organisation, known as the GP-TCM Research Association (see http://www.gp-tcm.org online). Launched in April 2012, the Association has officially succeeded the missions and legacies of the FP7 GP-TCM project since November 2012. It will remain a devoted link between EU, China and other parts of the world, especially dedicated to dissemination, validation and further development of good practice guidelines through interregional, interdisciplinary and intersectoral collaborations in TCM research.

It summary, due to its personalised and function-oriented features and its holistic and pre-emptive approaches, TCM is highly complementary to the current model of Western medicine and thus represents an important field for future research. Through face-to-face meetings, outreach events, teleconferences, project website (see http://project.gp-tcm.org/ online), newsletters (see http://www.gp-tcm.org/news-list/ online), dissemination reports in public media and scientific magazines, as well as 100 deliverable reports (see http://project.gp-tcm.org/about/deliverables/ online), the GP-TCM project widely disseminated good practice guidelines and met all the planned objectives and milestones.

Looking forward, prospects for the whole area largely depend on how experts in different disciplines and stakeholders in different regions and sectors collaborate and how much funding is invested into this field. To reach the goals of better quality, safety and efficacy in the future of TCM, the GP-TCM consortium proposes that the rules of integrity (good practice), integration (collaboration) and innovation must be followed.

References:

[1] Nestler, G., 2002. Traditional Chinese medicine. Med. Clin. North Am., 86(1): 63-73.
[2] Normile D., 2003. Asian medicine. The new face of traditional Chinese medicine. Science, 299(5604):188-90.
[3] Uzuner, H., Fan, T.-P., Dias, A., Guo, D.A., El-Nezami, H.S. and Xu, Q., 2010. Establishing an EU-China consortium on traditional Chinese medicine research. Chinese Medicine. 5, 42.
[4] Fisher, P. and Ward, A., 1994. Complementary medicine in Europe. BMJ 309, 107-111.
[5] Dobos, G. and Tao, I., 2011. The model of Western integrative medicine: the role of Chinese medicine. Chinese Journal of Integrative Medicine. 17, 11-20.
[6] Uzuner H., Bauer, R., Fan, T.-P., Guo, D., Dias, A., El-Nezami, H., Efferth, T., Williamson, E.M., Heinrich, M., Robinson, N., Hylands, P.J., Hendry, B.M., Cheng, Y-C. Xu, Q., 2012. Traditional Chinese medicine research in the post-genomic era: Good practice, priorities, challenges and opportunities, Journal of Ethnopharmacology, Volume 140, Issue 3, Pages 458-468.

Project Context and Objectives:
4.1.2 Summary description of project context and objectives:

In recent years, TCM has been increasingly used in Europe [3,4,5]. However, in contrast to the reductionist approach of Western medicine that is based on anatomy, physiology, pharmacology, cell and molecular biology, TCM is based on thousands of years of recorded clinical experience, guided by Chinese philosophy, e.g. the Yin-Yang theory emphasising the balance of functional systems. TCM uses a theoretical system with a personalised and holistic approach to describe health and disease [2]. Speaking in metaphors, while Western medicine tends to see trees but not the wood, TCM, on the other hand, often sees the wood but not the trees. Therefore, both systems can learn from each other.

On 1st May 2009, the GP-TCM project was launched as the first EU-funded FP7 consortium, aiming to inform the best practice and harmonise research into TCM through interregional, interdisciplinary and intersectoral collaboration. In TCM, CHM and acupuncture are the most commonly used and thus each formed a focus for the current project. With a total budget of approximately 1 million Euro, the project especially emphasised the application of omics and systems biology technologies. The suffix omics was defined by the consortium as a description of various technical approaches of the post-genomic era, addressing whole profiles of DNA (genomics), mRNA (transcriptomics), proteins (proteomics), metabolites (metabolomics/metabonomics) through comprehensive bioinformatics-based analysis [7]. These technologies and related functional measurements, collectively known as functional genomics, allow information-rich and high-throughput molecular observations, aiming to link them to biologically and clinically relevant functions using a systems biology approach. Therefore, the central hypothesis of the consortium was that, using functional genomics technology, which allows high-content observations of whole profiles of molecules at different levels, i.e. DNA, mRNA, protein, metabolites, etc., and furthermore links them to clinically relevant biological functions, we might be in a better position than ever before to interpret and validate the scientific value of TCM in a holistic and function-oriented manner.

During its 3.5-year programme, the GP-TCM project focussed on a number of important pan-European activities that led to achieve agreement and support best quality TCM research: agreement on CHM terminology, CHM extraction and analysis protocols, best quality control criteria, priority areas of future research, etc. At the same time, the consortium acted as the main pan-European facilitator of TCM research cross-border fora and collaborations within and beyond Europe, and assisted bridging Chinese and Western medicines while developing and promoting good practice.

The consortium aimed to address good practice issues related to various aspects of CHM and acupuncture research, leading to state-of-the-art reports, guidelines and consensus on the application of omic technologies in TCM research. The consortium's main activities were designed to support establishing and expanding TCM research network by performing literature reviews, encouraging discussions, identifying knowledge gaps, developing methodologies and standardised protocols to achieve good practice in TCM research, identifying priority areas for future direction of research, creating online resources such as reports, reviewing articles, developing databases to help establish new knowledge and supporting/informing scientists and the public, and finally establishing

a new association to sustain the coordination of TCM research in and beyond Europe. While informing the best practice, GP-TCM also aimed to harmonise research on the safety and efficacy of TCM in EU member states through exchange of opinions, experience and expertise among scientists.

According to the Technical Annex of the project, the overall objectives and the scientific and technological objectives of the project can be summarised as follows.

Objective 1 To develop a European-Chinese network collaborating on functional genomics research in TCM;
Objective 2 To review current practice of TCM research, identifying problems and proposing ways out;
Objective 3 To propose standard protocols of methodology;
Objective 4 To propose priority areas of future research;
Objective 5 To develop online resources to support and enhance Pan-European studies of TCM research;
Objective 6 To facilitate and foster sustainable good practice research and European-Chinese collaboration by founding The GP-TCM Research Association.

Objective 1 To identify the cultural and legal differences in the EU member states and China, with respect to TCM, and propose strategies to promote mutual understanding and collaboration;
Objective 2 To identify problems of European scientists within TCM research and propose potential ways to resolve these issues, especially using functional genomics approach;
Objective 3 To formulate protocols for best practice in herbal medicine and acupuncture research;
Objective 4 To identify and prioritise diseases for which herbal medicines or acupuncture may have convincing clinical efficacy;
Objective 5 To identify Chinese herbal medicines that are most likely to present breakthroughs in clinical practice in the EU;
Objective 6 To stimulate interaction among TCM practitioners, clinicians, animal experimentalists, cell biologists, toxicologists, pharmacologists and experts of functional genomics to identify priority areas of TCM that functional genomics might bring forth breakthroughs;
Objective 7 To establish websites, online protocols and Bulletin Board System (BBS) talk shops to promote dissemination of experience and expertise in TCM research in a coordinated way;
Objective 8 To found the GP-TCM Research Association, which aims to foster sustainable rigorous TCM research within and beyond the EU.

Thanks to the joint efforts by consortium partners and stakeholders, the project successfully met all the above overall and scientific and technological objectives as planned, when the project was officially concluded on 31st October 2012.

- A large European-Chinese network collaborating on functional genomics research of TCM was developed and further expanded to cover not only Europe and China but also other parts of the world.
- The experts were brought together in speciality groups or in consortium-wide activities either face to face, through teleconferences or other forms of telecommunications to facilitate discussions and to promote mutual understanding and collaborations.

- Current practice of TCM research was reviewed, problems identified, and solutions proposed.
- Standard protocols and methodology were proposed.
- The application of emerging technologies such as functional genomics in TCM research was evaluated.
- Priority, challenges and opportunities in future TCM research were proposed.
- Website, newsletters, databases and other online resources to support and enhance Pan-European studies of TCM research were developed.
- The GP-TCM Research Association was established to facilitate and foster sustainable good practice research and European-Chinese collaboration.

References:

[7] Joyce, A.R. and Palsson, B.O., 2006. The model organism as a system: integrating 'omics' data sets. Nature Reviews Molecular Cell Biology. 7, 198-210.

Project Results:
4.1.3 Description of the main S&T (Science and Technology) results/foregrounds:

By 31st October 2012, through 3.5 years of team building, the GP-TCM consortium had grown into a large collaborative network involving approximately 200 scientists from 24 countries and 110 institutions.

The consortium had 29 beneficiary partners (i.e. the contractors) across 10 EU member states (Austria, Belgium, Estonia, Germany, Ireland, Italy, the Netherlands, Portugal, Spain and UK) and China, an International Cooperation Partner Country (ICPC). In addition, the consortium had additional 80 non-beneficiary partner organisations as well as 2 independent experts from Australia, Austria, Belgium, Burkina Faso, Canada, China, Democratic Republic of Congo, Denmark, Finland, Germany, Italy, Luxembourg, the Netherlands, Norway, Romania, Russia, Spain, Sweden, Thailand, UK and USA. Please refer to the attached document entitled "D10-5-Part4-Lists of members.pdf" for the full list of consortium partners. The consortium partnership spanned across both the public (approximately 80%) and private sectors (approximately 20%) and all members had a proven track record and an international reputation in TCM related research.

GP-TCM comprised 10 interactive WPs. Through 10 WPs, the consortium took actions to review the techniques, identify problems and solutions in the quality control (WP1), extraction and analysis (WP2) of CHMs. While these fundamental issues were addressed, discussion fora emphasising the use of functional genomics methodology in research of the safety, efficacy and mechanisms of CHMs (WP3-WP7) and acupuncture (WP8) formed the core of this coordination project. The project covered toxicology (WP3), in vitro, in vivo and clinical pharmacology (WP4-WP6), as well as industrial R&D and international regulatory issues of CHM (WP7). WP9 was dedicated to organise the Final Conference of the consortium and the GP-TCM Congress (an international public dissemination event) at the end of the project. WP10 was in charge of managing consortium-wide matters, such as appointment and coordination of WP leadership, recruitment of additional experts, editing website and newsletters, drafting standard operating procedures, providing scientific and technological support and guidance, organising internal review and quality assurance, collation, integration and dissemination of results, as well as liaison with the Commission and other stakeholders and external authorities.

The project activities and management was overseen by a Coordination Office and a Steering Committee, which were supported by an Advisory Board, a Scientific and Technological Advisory Committee, a Literature Review Standard Operating Procedure (SOP) Panel (also known as the Literature Review Good Practice Panel) and an Ethics Panel.

Consortium's 10 independent but interactive WPs all included both specialists of TCM research and experts of functional genomics. WPs and their activities were led by world-renowned institutions and scientists, as follows.

WP no. WP title Lead institution * (country) WP Lead
WP1 Quality control of CHM Kew (UK) Prof. Monique Simmonds
WP2 Extraction and component analysis of CHM HHU (Germany) Prof. Peter Proksch and Dr. Jandirk Sendker

WP3 Functional genomics in toxicology study of CHM ULB (Belgium) and IMPLAD (China) Prof. Pierre Duez and Prof. Xinmin Liu
WP4 Functional genomics of CHM research in vitro KCL (UK) Prof. Peter Hylands
WP5 Functional genomics studies of CHM in vivo UA (Spain) Prof. Javier Lucio-Cazaña
WP6 Functional genomics in clinical studies of CHM LSBU (UK) Prof. Nicola Robinson and Prof. Ken Muir
WP7 Functional genomics in R&D of CHM UCAM (UK) and UoW (UK) Dr. Tai-Ping Fan and Prof. Kelvin Chan
WP8 Functional genomics in studies of acupuncture-moxibustion CCMU (China) and LSBU (UK) Prof. Xiaomin Wang and Prof. Nicola Robinson
WP9 Final Conference LU (the Netherlands) Prof. Rob Verpoorte
WP10 Management KCL (UK) Dr. Qihe Xu

Over the past 3.5 years, all 10 WPs worked diligently together on TCM literature research and discussions of good practice issues. Collectively, GP-TCM partners formed a strong and sustainable pan-European TCM research network, established and maintained important links with TCM and functional genomics experts in Europe, China and other parts of the world.
The consortium played a keen role in receiving internal and external evidence to support improving guidelines and define even better practice. The critical importance of disseminating project outcomes and receiving feedback from broader scientific communities and stakeholders were emphasised. In particular, GP-TCM was in liaison with a number of key stakeholders and international organisations such as the European Directorate for the Quality of Medicines and Healthcare (EDQM) TCM Working Party, the European Medicines Agency (EMA) Committee on Herbal Medicinal Products (HMPC), the China State Administration of TCM (SATCM), the Chinese Pharmacopoeia TCM Commission, the China Science and Technology Exchange Centre, China's Ministry of Science and Technology (MOST), the Consortium for Globalization of Chinese Medicine (CGCM), and various TCM practitioner bodies in different countries, etc. As research into many other systems of traditional medicines equally needs good practice guidelines, the consortium also collaborated with many colleagues outside the EU and China, including the US Food and Drug Administration (FDA) Botanical Review Team.

Good practice was the soul of the GP-TCM consortium. The consortium produced a broad definition to good practice as compliance with the European Charter for Researchers, the European Agency for Safety and Health at Work Guidelines, commonly accepted guidelines for medical research, such as the Wellcome Trust Guidelines on Good Research Practice, as well as a definition of good practice from the European Institute for Comparative Cultural Research. In addition, good practice was defined technically as good practice guidelines needed for all aspects of TCM research; strategically, it was defined as collaboration and share; and practically, it was defined as striving for consensus while respecting differences of opinion [6].

For example, to develop easy-to-follow guidelines and to support the whole consortium, a Literature Review Good Practice Panel was established, which led the identification of common problems, while conducting focused discussions and proposing solutions. As a result, good practice guidelines on reviewing and publishing herbal studies, with special emphasis on TCM and Chinese materia medica, were developed and published in the GP-TCM Journal of Ethnopharmacology special issue.

By producing consortium-wide and WP-based recommendations, the directions for future research and funding were collectively identified and disseminated for wider discussions, validations and action. At the end of its funded lifetime, the consortium successfully completed all its deliverables and met its milestones across all WPs.

As a result of joint activities such as regular meetings, discussion fora and literature studies, the consortium reached agreement on guidelines for reviewing and publishing TCM literature, naming and authentication of medical plants, evaluating the impact of different extraction methods in TCM clinical practice and in research, and for conducting clinical trials on CHM. It also compiled a comprehensive comparison of global regulation on CHM. The consortium studied the state of the art of CHM and acupuncture research and paid keen attention to the application of omics and systems biology methodologies in TCM research. Close collaborations were forged with other interested TCM research organisations in order to avoid duplicating effort and to produce a greater impact by working together. Large numbers of public access reports as well as review articles were published to support online resource development.

In summary, the consortium delivered the following outcomes, which will continue to have impact on EU and international science and policy-making arenas beyond its funded lifetime:

- The open-access GP-TCM Journal of Ethnopharmacology Special Issue as a collection of authoritative references on state of the art and guidelines:
http://www.sciencedirect.com/science/journal/03788741/140

- The GP-TCM Research Association, a new international society dedicated to dissemination, validation and further development of good practices and sustainable coordination of EU-China collaboration in TCM research:
http://www.GP-TCM.org/

- International expert networks focusing on EU-China collaborations in TCM research, which will continue to collaborate beyond the funded lifetime of the project in their respective fields (attached supplementary document entitled - "D10-5-Part4-List of members);

- Freely available new knowledge via opinion polls, comprehensive reports and review articles addressing fundamental issues in TCM research, including omic research of TCM (Part 4.2A1 - List of scientific publications)
http://project.GP-TCM.org/2011/08/"grand-priorities-challenges-and-opportunities"-survey/

- Freely available good practice guidelines and handbooks for reviewing and publishing TCM research:
http://www.sciencedirect.com/science/article/pii/S0378874112000517

- Freely available guidelines on clinical studies of TCM and CHM:
http://www.GP-TCM.org/2012/12/GP-TCM-guidelines-for-randomized-controlled-trials-investigating-chinese-herbal-medicine-chm-2/
http://www.sciencedirect.com/science/article/pii/S0378874111008956

- Increased visibility of EU-China collaboration in TCM research to governments and non-governmental organisations in Europe, China and

beyond through dissemination activities (Part 4.2A2 - List of dissemination activities);

- New grant applications and successful awards due to the GP-TCM collaboration, such as a EU-funded project entitled Discovery of bioactive natural compounds from Traditional Chinese Medicines used against Cardiovascular Disease (TCM-VASC) and two more projects entitled Neuro-biological mechanism of KXS on memory enhancement and Research of effective components from Polygala tenuifolia on improving learning and memory in vivo funded by MOST, China;

- Enhanced level of collaborations between European partners, as well as between European and Chinese institutions, such as between King's College London (UK) and Chengdu University of TCM (China); between China Academy of Chinese Medical Sciences (CACMS, China) and The Norwegian University of Science and Technology (NTNU, Norway); and between Shanghai Research Centre for TCM Modernization, Shanghai Institute of Materia Medica, Chinese Academy of Sciences (China) and the Institute of Pharmaceutical Sciences, Department of Pharmacognosy, Karl-Franzens-University Graz (Austria).

The consortium has paid keen attention to disseminate its findings and outcomes through organising international conferences such as the Sino-EU GP-TCM Workshop in Beijing, China (2009), the 1st Annual Meeting in Henley, UK (2010), the 2nd Annual Meeting in Braga, Portugal (2011), the GP-TCM Final Conference in Kerkrade, the Netherlands (2012), the GP-TCM Congress in Leiden, the Netherlands (2012), the 2012 Shanghai International Conference on TCM and Natural Medicine and the GP-TCM Research Association First Annual Meeting in Shanghai, China (2012) and the International Symposium on Standardisation and Cooperation of TCM in Beijing, China (2012), as well as delivering talks and posters in other conferences, workshops and seminars, or displaying and circulating leaflets, newsletters and being interviewed by public media such as newsletters, radio and TV programmes.

The following sections provide summaries to each WP's focuses, activities and outcomes.

1.3.1 WP1 - Quality Control of CHM

Objectives: The main objectives of WP1 were to design a standard system to review the literature on papers associated with plants used in CHM and use the information gained from this review to develop a system for the quality control of CHM in the EU. The system will take into account what is known about the complexity of CHM such as the nomenclature, the need to ensure plants had been identified correctly and that researchers were aware of the complexity of the different names that could be used to describe a species. This information is needed to improving data gathering on species used in CHM. The final aim was to provide guidelines to support the rational development of research methods to authenticate and monitor the quality of CHM plants entering the trade. Guidelines will aim to avoid duplication of research efforts and maximise the use of modern molecular and chemical techniques, especially a functional genomic approach. The aims of WP1 were closely aligned with those of WP2 and WP4.

Description of work: A group of specialists in different aspects of the quality control of TCM plants from the EU and China was brought together

in a series of one-to-one meetings and telephone meetings. Because the aims of WP1 were closely aligned with those of WP2 and WP4, joint meeting took place between the groups during the three years of the projects. WP1 was initially going to review the literature on the top 100 plants entering the EU and then narrow the range of species to 20-40 as outlined in the project proposal. However, it was decided at the first Annual Conference at Henley to concentrate on gathering data about the plants as used in CHM formula. A formula that is commonly used in China was selected and then research was undertaken into what is known about the quality control of the formulae as well as the individual species used in the formulae. The formula selected was Liu Wei Di Huang Wan which contains 5 plants and a fungus. Each species is known to have substitutes and adulterants so the total number of species studies was over 40. This also included other species of interest to the other WPs. The findings showed that although the number of references about each species varies greatly depending on the search engine used and the terms used to search the literature, few contained robust data about the botanical aspects and chemistry of the plants and the extracts being tested. What is clear is that there is very little scientific information in these papers about what the quality should be of the six plants/fungi used in Liu Wei Di Huang Wan. For some plants there is a wealth of scientific information about the chemistry of the plants and their proposed and actual medicinal properties. However, very few of these publications link directly back to the traditional use of the plant as used in Liu Wei Di Huang Wan. The formula was selected because it is widely used in China and thus it was assumed that the uses would be supported by publications. The data gathered during the study illustrated the need for more targeted research on the plants and the formula to support the use of the plants in EU.

Data about the nomenclatural issues, the chemistry and medicinal properties of the target plants assessed from reviewing 1000 publications including the 400 reviewed with WP2. The task of reviewing the literature on the selected species was allocated among the members of WP1. The Royal Botanic Gardens, Kew provided information about the Latin botanical names for the plants and members of the team provided information about the pharmaceutical and Chinese names. These names were used to search databases for information about the plants. The main databases used were PubMed, Web of Science and Google Scholar. Information was also obtained from the Chinese pharmacopeia. The reviews evaluated whether the authors had identified the plants they were working on, whether they had deposited a voucher of the samples they worked on. In many cases the researchers worked on plant material obtained from markets and the plant material was not verified. Another issue identified by the review was the lack of knowledge about the chemistry of the samples they tested. For example, authors might evaluate the anti-inflammatory activity of a species but they did not provide any information about the chemical profile of the plant-derived extracts they tested. In other cases the papers did not relate directly to the traditional uses of the plants. The results of reviewing over 1000 publications identified that there are many gaps in our knowledge about what the chemical profile (profile of compounds and relative concentrations) of a good quality plant is and how these plants should be grown. However, there was data available about the cultivation of the plants used in Liu Wei Di Huang Wan. Some of the gaps in the chemical and efficacy data could most likely be filled by a more intensive review of the Chinese literature, especially in books or standard operating procedures used by the manufactures of the Liu Wei Di Huang Wan product. However, this literature was not easy to obtain. Thus a review of the literature shows that for some species there is very

little relevant information available about the criteria for quality control in the academic literature outside China.

Outcomes:

- 4 reports on the activities of WP1;
- A database that provides information about the names of the plants used in Liu Wei Di Huang Wan that is available on the GP-TCM website;
- A presentation at the 2012 meeting in Leiden;
- Two review articles:
  - Chan K, Shaw D, Simmonds MS, Leon CJ, Xu Q, Lu A, Sutherland I, Ignatova S, Zhu YP, Verpoorte R, Williamson EM, Duez P. Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on Traditional Chinese Medicine and Chinese Materia Medica. J Ethnopharmacol. 2012; 140: 469-475.
  - Zhao Z, Guo P, Brand E. The formation of daodi medicinal materials. J Ethnopharmacol. 2012; 140: 476-481.

Priority areas:

- The production of a database that brings together the Latin accepted scientific binomial names of the plants, synonyms, pharmaceutical and Chinese names;
- Research that further our understanding of the chemical profile of a quality plant based on a better understanding of the pharmacology of the extracts tested;
- Improved understanding of the agricultural practices needed to produce good quality place;
- Better understanding of the supply chain of the plant used in TCM to ensure that there are plentiful supplies of quality plants obtained from sustainably harvested sources;
- Development of molecular methods (DNA and chemical) that can be used to identify species and enable the identification of substitutes and adulterants.

1.3.2 WP2 - Extraction and Component Analysis of CHM

Objectives: The objectives of WP2 were situated around the extraction and component analysis of CHMs. In general, the currently employed traditional extraction technologies had to be evaluated with regard to special phytochemical characteristics of CHM. Problems and gaps of knowledge that need to be addressed for a reasonable modernisation of the traditional preparations towards more convenient application forms had to be identified. This comprised describing and evaluating both traditional and modern extraction and drug processing procedures as well the techniques for the chemical characterisation of the extracts and to connect the chemical properties to their biological activity. Moreover, the potential of modern analytical and data processing techniques to approach the identified gaps of knowledge, i.e. missing information about the active and hence quality-determining chemical components, was to be evaluated. The phytochemical focus of WP2 was closely related to parts of the work of WP1, which resulted in close collaboration of both WPs.

Description of work: Due to the close relation between WP1 and WP2 that had been figured out early in the project, WP2 started its activities with a joint workshop with WP1 in London. On that occasion the joint compilation of plant-species-related literature data was identified as a field of mutual collaboration between the WPs. This collaboration

continued in the organisation of further joint face-to-face meetings and telecommunication events throughout the project's lifetime. The methodology and analytical techniques applied in research on extract chemistry of TCM herbal drugs were studied based on a literature research of original scientific publications on 20 TCM plant species. Further, the currently applied techniques for extraction but also for processing of plant material were studied and discussed during the second joint WP1/WP2 workshop in Düsseldorf. It turned out that already the protocols for traditional tang decoctions with water, which make an overwhelming part of the traditional applications, show numerous variations in dependence of the herbal drugs involved. It became evident that this complex variability and special features like the so-called paozhi processing represent very specific aspects of TCM. Their potential to impact on an extract's chemical composition is not at all appropriately recognised by scientific literature or pharmacopoeia monographs.

Consequently a detailed research of present scientific literature was performed together with WP1 with a selection of the consortium-wide priority list of plant species that had been established concurrently. As this literature research was intended to be a gap-analysis, original scientific publications had to be screened systematically for their content of very particular information. Therefore, an MS-Excel-based survey form was designed to collect information from the reviewed publications. The form predominantly worked with lists of preformed entries to choose from for each aspect of interest. Defining the aspects of interest and the preformed entries was of major importance for the success of the procedure; major parts of this were done during a joint WP1/WP2 workshop in Braga. Together with the literature scoring system described in the consortium's literature review SOP, this procedure allowed to analyse the literature data for gaps of information, i.e. quality of information on botanical origin, processing of plant material, extraction procedures, methods of chemical extract characterisation, connection between activity and chemical composition. The raw data from these forms (altogether 400 entries were contributed by the participants, each representing one original scientific publication) were processed using Pivot-Tables thereby counting and comparing numbers of publications with specific attributes. Typical information extractable from the matrix of literature data was e.g. that 9% of the publications describing an extract's pharmacological activity chemically characterised the extract using HPLC while 47% did not chemically characterise the extract at all. This literature analysis also revealed a number of specific problems and non-standard-areas that were consecutively addressed in more detail.

Parallel to this large literature survey, WP2 dealt with modern analytical and data processing techniques that are suitable to systematically identify relevant chemical components from the extremely complex matrices deriving from multiple herbal ingredients of a CHM. An initial discussion on the general methodology of metabolomics and its potential for the research on traditional herbal medicines took place during the third joint WP1/WP2 workshop in Braga. Existing examples of metabolomics studies based on hyphenated analytical techniques and methods of multivariate statistics were evaluated for their potential to address the problems and gaps of knowledge identified by the previous literature survey.

The outcomes of these basic deliverables were discussed in order to define the priority problems/gaps of knowledge and to address them for future directions of research and funding.

Outcomes: Traditional CHM preparations, mainly elaborative decoctions of complex herbal mixtures with water, are more and more replaced by modernised and more convenient products like granules that are just to be suspended in water before application. However, there is lack of evidence that such preparations are comparable with their traditional prototypes in terms of activity and chemical composition. Before a traditional tang decoction is administered, its constituents undergo a number of treatments like drying, wet-cutting, or paozhi processing; the extraction is then usually performed as a co-extraction of multiple herbal ingredients which may additionally undergo a period of soaking in cold water. While any of the mentioned processes are influencing the final extract's chemical composition (e.g. by fermentation processes during wet cutting or soaking in cold water), the overall knowledge about their factual impact must be considered as poor. Moreover, these processes are widely disregarded when characterising an herbal specimen in the context of activity studies. In particular, the TCM specific processes of wet-cutting and paozhi processing must be considered as common practice in application, but are almost completely neglected in activity studies of CHM. We found the practice of co-extraction to be a matter of major importance: while widely untouched from systematic research approaches, a series of detailed studies on the rather simple two-herb-preparation danggui buxue tang indicates major interactions between the two herbal materials. These interactions lead to significant variations in both the chemical composition and the biological activity in dependence of the ratio of herbal ingredients, extraction details, possible paozhi treatment and the protocol for preparing a dry extract. As the TCM herbal mixtures and their processing and extraction protocols are claimed to be the result of a several-thousand-years process that led to optimised products, knowledge about the chemical background and potential interactions between components is an important prerequisite for the identification of relevant, quality determining phytochemicals and hence for a rational modernisation of CHM based on traditional knowledge and experience.

The outcomes are represented by the WP2 deliverables, including dissemination (Review paper published in Journal of Ethnopharmacology and presentation of results on an International conference).

Priority areas:

- Comparative studies on the activity and chemical composition of traditional and modernised extracts of CHM;

- Elucidation of the impact of traditional post-harvest processing techniques (drying, wet-cutting, paozhi, soaking in cold water, co-extraction) on the product's chemical profile using metabolomic techniques;

- Identification of quality determining chemical components from traditionally prepared CHM taking advantage of the rich traditional variability of TCM drugs for the application of activity-guided metabolomic techniques;

- Simplification of complex traditional preparations by (i) identification and removal of dispensable herbal ingredients and (ii) identification and deletion of dispensable methods of processing (please refer to deliverable D2.12 report for more details).

1.3.3 WP3 - Functional Genomics in Toxicology Study of CHM

Objectives: The research protocols, standards and methods for the evaluation of the safety and efficacy of TCM, including CHM, are more complex than those for conventional medicines. Indeed, TCM presents a unique set of pharmaceutical theories that include particular methods for processing, combining and decocting CHM, which probably contribute to reduce their eventual toxicity and enhance their efficacy. The evaluation of CHM safety is complicated by multiple factors, such as the geographical origin of plant material, different processing techniques, dosage, route of administration and compatibility with other medicines. As a first objective, WP3 aimed at reviewing the application to CHM of safety evaluation methods that combine newly evolved and rapidly developing techniques, especially functional genomics, with essential animal, cell culture and molecular biology experiments; this part of the literature search was centred on methods and related to prototype toxicants ("prototoxicants").

A second objective aimed at understanding the current status of toxicological knowledge on CHM (adverse effects and safety, including genotoxicity, teratogenicity, neurotoxicity, nephrotoxicity, hepatotoxicity). This part of the literature search (adverse effects and safety) was conducted on a series of "typical" CHM selected after examination of various herbs lists. The selection included "top-seller" plants and known toxic plants.

A third topic aimed at determining what is available in terms of pharmacovigilance and herb-drug interaction data. Making sense of existing reports is a very important topic, even more so, since the most useful pharmacotoxicological tests predictive for clinical relevance are not known. The priorities for WP3 were forming network, sharing experiences and information on the current status of toxicity of Chinese herbal medicine, between EU and Chinese scientists. The perception of safety issues by "consumers" was then investigated both in EU and China.

Description of work:

- To achieve its intended goals, the WP3 group has established a network of experts in the field, which has been strengthened all along the project duration. WP3 has developed a series of literature searches;

- The WP3 kick-off meeting, "Functional genomics and toxicological studies applied to TCM", was held on 24th and 25th October 2009 in Brussels La Hulpe, bringing together 8 WP3 groups from both China and Europe (out of a total of 13 groups), the Coordinator of WP5 and 3 guests from Belgium and D. R. Congo; Xinmin Liu has organised 5 mini-workshops for Chinese participants in Beijing to draft WP3 plans;

- A series of e-mail contacts circulated lists of plants and composed preparations, thanks to Dr. You-Ping Zhu (China-Netherlands Medical and Pharmaceutical Centre, NEDICHIN BV, The Netherlands), Prof. Benny Mei of ACUMED, London UK, Kelvin Chan, Xinmin Liu, Yanjiang Qiao, Elizabeth Williamson and Debbie Shaw: Best selling herbs in Europe, top 15 PCM in Europe, PCM substitutable by aristolochic acids containing herbs, herbs associated with unpredictable hepatotoxicity, herbs from the "973 programme";

- Three web-based meetings were organised and frequent exchanges of e-mails between all WP3 members allowed to discuss the finalisation of deliverables, to prepare the final WP3 reports, to prepare the Henley (1st AGM), Braga (2nd AGM) and final conferences, to obtain feedback on the drafts for the SOP literature panel, to move on the different reviewing topics, to assign tasks to WP3 members and to define the organisation of the work for "systematic literature review and translation";

- A survey on the perception of safety by stakeholders was designed, launched and analysed by Prof. Pierre Duez and his team for deliverable D3.6, with support from number of WP3 members;

- Hani El-Nezami, Joëlle Nortier, Pierre Duez, Jue Zhou, Fan Qu and Caroline Stévigny have coordinated literature reviewing on some toxicities by PhD and master students;

- A joint workshop was organised with WP1, WP3, and WP7 members and experts of the EDQM European Pharmacopoeia TCM workgroup (Strasbourg, France, 29th September 2011). Prof. Duez presented a short talk: "GP-TCM – Introduction and brief progress of WP3";

- A workshop was organised (September 2011) by Prof. Xinmin Liu in Luzhou Medical College, Sichuan Province, China, for discussing review manuscripts on toxicity of CHMs;

- Prof. Xinmin Liu introduced GP-TCM to Mr Yu Wenming, Deputy General-Director of SATCM, Ms. Xiaopin Wang, Director of Department of International Cooperation of SATCM, Dr. Jijun Xing, Deputy Director of China Science and Technology Exchange Centre, MOST and Dr. Philippe Vialatte, the representative from Science and Technology Section, EU Delegation in China;

- Prof. Duez organised a 3-months writing session for WP3 reviews, jointly with M. Ouédraogo, C. Stévigny, J. Nortier and T. Baudoux;

- Prof. Xinmin Liu helped the Hunan University of TCM in Changsha, Hunan, China, to set up "Sino-EU Contact Office (Traditional Medicine), with strong support from Dr. Jijun Xing, the Deputy Director of China Science and Technology Exchange Centre, MOST, China.

Outcomes:

WP3 has defined the meaning of "toxicity" with regard to its activities as follows: "Possible harmful reaction to the body which is not related to therapeutic effect. Toxicity can then be classified into (i) side effects (covered by pharmacodynamics and often predictable), (ii) reactions occurring as a result of overdose, over-duration, tolerance, dependence-addiction (covered either by pharmacodynamics and pharmacovigilance), (iii) hypersensitivity, allergic and idiosyncratic reaction (covered by pharmacovigilance), (iv) mid-term and long-term toxic effects (liver, renal, genotoxicity, teratogenecity, neurotoxicity, cardiotoxicity,…)". It has been agreed that point (iv) is the most important field for 'omics' predictive toxicology.

Talks at various meetings and symposiums by J. Nortier (1 in Taiwan), P. Duez (7 in Belgium, China, RD Congo, Syria, Vietnam) and O. Pelkonen (6

in Spain France, UK, Finland, Romania) allowed to present WP3 activities. Nine deliverables were prepared and three reviews were published.

New projects entitled "Neuro-biological mechanism of KXS on memory enhancement" and "Research of effective components from Polygala tenuifolia on improving learning and memory in vivo" have been funded by MOST, China.

Priority areas:

- Development and validation of screening methods to rapidly identify herbs that may raise safety concerns, focusing on medium- and long-term toxicities;
- Development of research methodology and protocols for evaluating toxicity and safety of Chinese herbal medicine, taking into account TCM characteristics such as combination of herbs and processing;
- Reinforcement of pharmacovigilance for herbals, including all marketing status (drugs, food supplements, etc);
- Training scientists to meet the challenges of toxicological evaluation of herbals.

1.3.4 WP4 - Functional Genomics of CHM Research in Vitro

Objectives: The aim was to define and propose standardisation of in-vitro systems and their use in functional genomics studies (all the so-called 'omic' techniques) of CHM. The aim was accomplished by developing a general strategy and then identifying and defining quality criteria and procedures. Particular attention was paid to establishing best practice criteria for research methods and reporting. This enabled a further objective of evaluation of existing publications. This approach was to be used similarly to evaluate the quality of existing databases and in-silico tools, and to establish guidelines for good practice in in-silico research in CHM research. A further objective was to set up a repository on CHM research in vitro and provide it to the public in dedicated web pages.

Description of work: The main activities performed by WP4 were concerned with establishing a multidisciplinary network of experts in the field of in-vitro CHM research, to propose good practice and guidelines in the field. This was achieved by holding a number of face-to-face meetings together with e-contacts and conference calls. In particular, the kick-off meetings were useful for networking and to establish a formal organisation and agenda, though the main outputs of the meetings were focused on contents and output strategies, resulting in proposed criteria for literature evaluation. These were then trialled in two different phases, to achieve a final version of the criteria for evaluation of in-vitro CHM pharmacology research articles. Among the start-up activities, the setting up of the WP4 web pages represented an important step achieved in collaboration with the project manager, to provide up-to-date information (work package objectives and activities, news, membership info, etc) (see http://project.GP-TCM.org/work-package/wp4/wp4-home/ online). WP4 members used every opportunity to hold operative meetings, but coordinated collective discussions via e-mails and personal contacts were also held in order to develop further the subjects and collect members' opinions and feedback. Discussion groups were thus organised via e-mail and led by the WP4 coordination unit, which allowed to produce several documents and scientific papers. Some meetings were able to be held jointly with those of other WPs.

One of the main achievements of WP4 is the scoring procedure optimised to evaluate the presentation of research information in scientific papers on CHM research in vitro. This procedure was optimised after several iterations. A final procedure was established and used to extrapolate guidelines for good practice in presenting scientific data in research journals which led to a handbook on good practice in the reporting of CHM experimental work and its dissemination on the web pages.

An online "public access" repository was then produced where scored and un-scored papers on in-vitro CHM can be listed. The repository contains the following searchable fields: article (title, authors, journal, year and pages); plant (scientific name of the main plant); WP4 reference member; plant/s used (if a phytocomplex from one or more plants are used); formula used (if a phytocomplex from a formula is used); purified molecules used (if single compounds are used); disease/s; molecular target/s and/or mechanisms investigated; score (optional). The online repository aims to become a user-friendly tool for all researchers in TCM and, eventually, an important reference for the scientific community. The repository will be constantly updated by WP4 with the material coming from reviewers of each section and will continue to be managed even after the end of the project, just like the rest of the web pages, by the emerging GP-TCM Research Association.

Guidelines for good practice in in-silico research into traditional Chinese medicines were also established by examining the different kinds of databases identified as relevant including those holding ethnobotanical and/or chemical and/or pharmacological and/or toxicological data on the herbs used in Chinese medicine, as well as those with data on known or potential molecular targets for the herbal constituents. The software tools considered relevant included programs that provide for virtual screening of natural product libraries and chemical libraries, pattern recognition, omic data visualisation and analysis, and text mining.

As with previous guidelines, a draft set of criteria for evaluation of in-silico tools for use in CHM research was prepared and circulated for consideration by the WP4 in-silico work-group; these criteria served to provide a focus for discussions at the consensus meeting. These Guidelines for good practice in in-silico research were then collected in a handbook, made available on the WP4 webpages.

An analysis of the state of the art of the application of functional genomics in in-vitro TCM research was carried on in the last months of the project among WP4 members. A questionnaire was also circulated among members addressing issues related to the use of omic techniques in TCM research. There was agreement that one single methodology cannot be considered sufficient to investigate mechanisms of action of CHM, and that a well-integrated pipeline should be used, comprising in-silico evaluation, in-vitro and in-vivo validation through a combination of classical biochemical signalling work, conventional molecular biology, omics technologies and bioinformatics. A handbook for using functional genomics techniques in in-vitro CHM research was also produced. The handbook provides for the first time guidelines for good practice in the application of these methods in CHM research.

The whole activity was also supported by a continuous examination of the existing literature on application of "omics" to CHM. This has also led to the production of two review papers and a scientific presentation.

Outcomes:

The WP4 outcomes are innovative insights in the field of "omics" applied to CHM research and their dissemination in the scientific community with reports, articles, on line resources and meetings (all the eighteen WP4 deliverables are available in the website), including 3 reports, 3 handbooks, a questionnaire survey, a dedicated webpage on WP4, a searchable database of critically reviewed and quality scored articles, a presentation at the 2012 meeting in Leiden, a review article (Omic techniques in systems biology approaches to traditional Chinese medicine research), and a review article (In-silico studies in Chinese herbal medicines' research: Evaluation of in-silico methodologies and phytochemical data sources), and a review of research to date.

In summary, the conclusions indicate that functional genomics, by combining results furnished through activity assays, genomics, proteomics, metabolomics, bioinformatics, and systems biology, is able to provide a wealth of interconnected and complementary data, and heralds an innovative, more "holistic" approach to herbal studies, making it closer to the holistic approaches underlying the practice of traditional Chinese medicine. Omic methodologies can be usefully applied to different phases of CHM research starting from standardisation and quality control of herbal formulae, characterisation of target-mediated and downstream effects, as well as identification of molecular mechanisms to predict side effects and interactions with other drugs. Thanks to their potential to unveil the interconnected pharmacological networks induced by complex herbal preparations, omic techniques can thus be considered powerful tools to address many open questions in CHM research. While all the omic techniques are slowly but firmly pushing their way further in CHM research, metabonomics seems to be rapidly gaining ground with respect to the others. This is probably due to the simplicity of the experimental design and its affordability, which allows direct and detailed analysis of large numbers of biological samples which, like urine, can easily be obtained. Metabonomics provides the possibility of examining complete metabolic pathways and their intermingled interactions in just one snapshot, taking a whole picture of the downstream outcomes of any biological perturbation. This would appear as the ultimate systems biology phenotyping and is particularly fit for studying TCM, with its holistic view of biological effects. Accordingly, not only metabonomics is used to study the action of Chinese formulae, but is being increasingly used to successfully characterise TCM syndromes.

Priority areas:

- Application of omics to CHM research;
- Encourage by all means possible the utilisation of the guidelines established in the WP work as standard for publication;
- TCM and pro-active approaches for prevention in the era of Personalised Medicine.

1.3.5 WP5 - Functional Genomics Studies of CHM in Vivo

Objectives: The aim of WP5 was to establish best practice for animal studies of CHM in the EU. This was achieved by examining the biomedical

literature on CHM in general and assessing the studies in animal models of selected diseases. Particular attention was paid to identify the most relevant methodological problems in these studies and to propose solutions, as well as to give directions for the application of functional genomics.

Description of work: To achieve the WP5 objectives, the group leadership built an expert network in CHM in animal models of disease. The WP5 kick-off meeting was held in Alcala de Henares University the days 2nd – 3rd June 2009 bringing together eleven WP5 members which discussed the 3-year plan of the WP and assigned jobs related to deliverables. Frequent e-contacts and personal contacts were helpful to establish the organisation and agenda, to discuss the relevant issues raised during the project and to agree criteria. We also established contacts with other WPs and, particularly, with WP3 (including attendance of WP5 coordinator to the WP3 kick-off meeting) since the work in animals is very relevant in Toxicology.
Following the WP5 kick-off meeting recommendations, the first main task of WP5 was to identify the general features of the CHM studies recorded in MEDLINE since 1950 in terms of language, impact factor, Country, most active areas of research, etc. The same study was also done in CHM studies involving animal models of disease. This work provided critical data on the most relevant characteristics of CHM research in general and in animal models of disease in particular (as compared to the features of research in allopathic medicine).
WP5 then analyzed the animal studies of CHM in relation to the need of scientific proof of the efficacy of CHM. To assess the pieces of evidence, the animal studies of CHM in English in six selected diseases were searched, which were chosen as samples of the whole field of animal studies of CHM. The diseases were cancer, diabetes mellitus, psoriasis, hypertension, fibrotic diseases and Alzheimer. Those CHM formulations from which there were at least two publications to support their efficacy in a given disease would be considered for further research.

In order to propose good practice and guidelines in the field, WP5 analysed a sample of 77 publications on CHM studies in animals in four disease areas: cancer, diabetes mellitus, Alzheimer and fibrotic diseases). To this end, they optimised a scoring procedure so that it was finally simplified in a check-list which allowed the quick evaluation of papers in order i) to detect the most frequent problems found in publications on animal studies of CHM (this would be particularly useful for a quick search of reproducible CHM treatment that is likely to be effective in a given disease, thereby allowing the generation of a priority list of candidate CHM for further research) and ii) to help design experiments devoid of the common problems found in the field. This was agreed to be a critical need for any study involving functional genomics technologies. The check-list was optimised in several steps comprising meetings and coordinated exchanges of papers, which were evaluated by different members and whose proposals were then compared, discussed and finally unified.

Outcomes: The main WP5 outcomes are as follows:
- Identification of the main features and trends of the studies of CHM recorded in MEDLINE, which special focus on the last decade and on studies in animal models of disease;
- Identification of the main problems in the experimental design of animal studies of CHM;

- Assessment of the scientific proof of the efficacy of CHM provided by animal studies;
- Provision of a checklist for i) the quick assessment of the quality of any animal study of CHM and ii) helping in the experimental design of new studies in animals through avoiding the most common methodological problems found in these studies;
- A presentation at the GP-TCM Congress held in Leiden (April 2012);
- 2 poster presentations in the 11th Congress of the International Society of Ethnopharmacology (Albacete, Spain, 2010: Animal Models for Cancer Research in TCM and Scientific Publications on Animal Studies of CHM and 1 poster presentation in the TCM Symposium (Braga, Portugal, 2011: State of the art in animal studies of CHM);
- One review article on: Omic techniques in systems biology approaches to traditional Chinese medicine research;
http://dx.doi.org/10.1016/j.jep.2012.01.055
- One review article on: Medline-based assessment of animal studies on Chinese herbal medicine. http://dx.doi.org/10.1016/j.jep.2012.02.008

Priority areas:
- Standardisation of the whole procedure of preparation of CHM formulations to be used in animal studies;
- Identification of key CHM for the treatment of selected diseases by getting proof of efficacy of selected CHM in comparable and reproducible animal studies;
- Application of omics to CHM research in animals.

1.3.6 WP6 - Functional Genomics in Clinical Studies of CHM

Objectives: The overall objectives for WP6 were to focus on reviewing current practice of CHM research, identifying problems and proposing solutions and to ensure that an unbiased view of current research in functional genomics of CHM was produced. This was to be achieved by initially establishing a European-Chinese partnership to in order to develop a clinical trial network in CHM. This expert group was to provide a platform to develop expert guidelines for clinical research and propose standard protocols on methodology for CHM trials.

A further key objective was to focus on defining areas of special interest for future CHM clinical research and propose priority areas for future research and clinical trials of CHM. This was to have a special emphasis on practical, safe and potentially effective areas that could provide opportunities to further informing future clinical practice for improving patient care.

Description of work: During the duration of the project, specific face-to-face meetings and teleconferences were held. The initial WP6 face-to-face kick off meeting was held on 8th October 2009 in Ascot, Berkshire, UK. At this meeting, there was agreement of tasks to be achieved between the participants. In addition, it was also agreed that WP6 should work in association with WP8 (acupuncture and moxibustion) to conduct a survey of TCM practice across Europe/China. WP6 members agreed to work together as a team under the WP6 leads to implement the specific objectives. The key tasks identified were:

- Carry out a survey on TCM practice and attitudes of good practice guidelines to the integration of complementary and alternative medicine and Western healthcare in the UK;

- Develop an international collaborative network for the development of clinical TCM studies;
- Review of the literature related to TCM in carefully chosen clinical studies in order to identify areas for future clinical research;
- Produce guidelines for clinical studies into TCM efficacy and functional genomics/metabolomics.

The success of WP6 was through the extensive contacts of WP6 members and contact with leading societies and individuals in the field. In particular, Professors Lewith/Witt and Dr. Flower had worked extensively with The International Society for Complementary Medicine, CAMbrella and the European Herbal Practitioners Association. These groups had significant components of their work focussed on Chinese and other herbal medicines. For the Pan European Federation of TCM and the Association of Traditional Medicine, Drs Huijun Shen and Dan Jiang facilitated close collaborations (Dr. Huijun Shen, President of the Association of TCM, UK). There were also links to The National Centre for Complementary and Alternative Medicine Research at the US National Institute of Health and to the Canadian equivalent (N-CAM). The long-term aim for this international network of expertise in clinical trials and Chinese herbal medicines was to build a network of high quality researchers interested in clinical studies and trials of TCM and herbal medicines.

In addition to the teleconferences, Face to Face meetings were held at at the 1st Annual General meeting of the consortium in Henley, UK and at the 2nd Annual General Meeting in Braga, Portugal, and the Final Conference in Kerkrade in Holland 12th – 13th April 2012. In addition, a specific joint WP6 / WP8 face-to-face meeting was held in Beijing in September 2011 in order to plan for the final year of the project and prioritise areas for future clinical research.

Outcomes:

- Established an international expert network with expertise in clinical trials and CHM to facilitate future clinical research collaborations and research planning.

- Two surveys were conducted. The first focused on good practice guidelines to ascertain their attitudes towards the integration of complementary and alternative medicines (CAM) and Western healthcare in a representative county in the UK. It also identified the availability of CAM including herbal medicines and acupuncture in primary care.
The second survey in conjunction with WP8 focused on TCM practitioners in EU and China and as well as identifying their perceptions of the evidence, safety and research priorities for future CHM research. CHM data has been analysed and a paper is currently being prepared for publication in Phytotherapy research.

- Provided clinical trial guidelines for the conduct of CHM trials for use by CHM researchers, in order to provide guidance and recommendations for good practice in CHM clinical trials. The full guidelines have been put on the GP-TCM website (internal pages) and a paper accepted into the special issue of the Journal of Ethnopharmacology.

- Reviewed the most recent evidence supporting CHM in some of the key selected conditions of interest to the WP6 members. This was not intended as a full systematic review of all published literature and did not include systematic reviews that were inconclusive. It also excludes

several hundred randomised controlled trials (RCT's) reported in journals of Chinese medicine but focused on systematic reviews published in the Cochrane library and other peer reviewed English language journals.

The review did not provide conclusive evidence of the effectiveness of CHM but provided preliminary evidence for the potential therapeutic benefit of CHM in the treatment of a wide range of medical conditions. It identified the important contributions to the evidence base to support the developing role of CHM in the provision of healthcare.

This exercise highlighted the barriers of accessing the Chinese literature and that this was an obstacle for any attempt at a genuine systematic review of CHM literature. This barrier can be overcome. It therefore remains very important to further integrate with our Chinese speaking researchers both in the West and within China.

An output of critical relevance to CHM was comparing differences in effectiveness and safety of CHM granules and decoctions and a systematic review was carried out. An article was prepared and accepted in the special issue of the Journal of Ethnopharmacology.

- Appraisal of literature on functional genomics. There was a lack of good quality studies in this area, and studies reviewed highlighted the general scope that such new approaches could offer. It was also recognised that the following were key issues to be addressed:
  - Authenticity and quality of plant material
  - Analysis of the mode of action of single plants and multi-component mixtures
  - Assessment of the toxicity of CHM
  - Drug metabolisation (individual drug responses)
- Ascertained topics areas for the future focus of CHM trials by engaging with TCM practitioners on defining priority areas.

Priority areas:

- Safety of CHM – Further research on adverse effects of CHM is required given a much lower reporting rate by Chinese practitioners;
- Key areas identified by CHM practitioners where more evidence is required suggested future areas where research should focus (obstetric/gynaecological complaints, dermatology and cancer);
- Conduct research on multi-herb formulae as used in clinical practice in conjunction with syndrome differentiation;
- Carry out further comparisons of different CHM preparations and methods of CHM delivery e.g. decoction, standardised formulae and semi standardised formulae using clinical trial methodology;
- Improve quality and reporting of clinical trials by the publication of trial protocols and ensuring voucher identification of CHM specimens.

1.3.7 WP7 - Functional Genomics in Research and Development(R&D) of CHM

Objectives: The overall objective for WP7 was to establish a collaborative network towards formulating an easy-to-follow statement on the various regulatory frameworks, with emphasising the synergies and highlighting the differences with the aim of helping to establish a universal harmonised regulatory framework for botanicals.
A further key objective was to focus on searching literature beyond herbal products and summarise what has been reported on the application of "omics" and functional genomics in R & D and regulation of any drugs

and then discuss its implications on R & D and regulation of CHM and other complex herbal products (CHP).

Description of work: In order to achieve the objectives of WP7, a WP7 face-to-face kick off meeting was held in 2 phases: Phase 1 held at Brunel Institute of Bioengineering, Brunel University, London (31st August to 1st September 2009), and Phase 2 held at King's College London (25th-26th July 2010). During interim teleconferences and annual meetings specific checkpoints were inspected, status of deliverables was surveyed and tasks were checked, defined and further focused, if needed. Changes in WP7 membership necessitated quite crucial reorganizations and delineations of objectives and tasks.

WP7 members collated regulatory data and drew comparison among different countries. Case studies were also created to illustrate the problems involved in registering TCM products in different regions worldwide. The Botanical Guidelines in the United States (FDA = Food and Drug Administration) and equivalent guidelines in Australia (TGA = Therapeutic Goods Administration), Canada (NHPD = Natural Health Products Directorate) and other territories (e.g. SE Asia, India, Russia, Africa and South America) were thoroughly analysed. The WP7 also acted as the interface with regulatory agencies in the European Union (EMA = European Medicines Agency) and China (SFDA = State Food and Drug Administration) as well as other regulatory agencies. Such interface allowed our members to discuss the problems and solutions in developing Chinese materia medica as proprietary Chinese herbal medicines that meet the market-entry standard. Literature search was also done beyond herbal products and it was summarised what has been reported on the application of "omics" in regulation of any drugs and then discuss its implications on regulation of CHP and CHM.

Through the effort of all WP7 members, regular communication with WP7 members and external experts was maintained. The work done allowed us to discuss and write a perspective on utility of functional genomics in CHM research and development and potentially in future regulation.

Outcomes:

The task to collect, organise, compare and summarize data on the regulation of herbal medicinal products, including TCM, in different parts of the world was focused on writing a reader-friendly document highlighting the complexity of the regulatory issues for registration of herbal products worldwide. The lessons learnt from global regulation of TCM provide valuable insights for regulation of other traditional medicine such as Ayurveda and Unani medicine, as well as other forms of indigenous medicine.

As the key deliverables of WP7, two major papers were published in the GP-TCM theme issue in Journal of Ethnopharmacology. The first one is a comprehensive summary of different herbal regulations worldwide titled Future development of global regulations of Chinese herbal products, which provides an updated information to researchers, regulatory authorities as well as industry worldwide.

Another publication was a perspective article entitled Omics and its potential impact on R&D and regulation of complex herbal products, which discussed about the utility of functional genomics in CHM research and development. It is important because functional genomics or omic

approaches are not yet obligatory parts of any dossiers in any regulatory framework. The principal conclusion of the task group was, however, that functional genomics approach would almost certainly be an instrumental tool for R & D and ultimately for regulatory acceptance, of CHM.

Other outcomes: WP7 Co-Coordinator Tai-Ping Fan announced that as a legacy for GP-TCM, he has been invited by American Association for the Advancement of Science magazine Science to edit a special sponsored issue on TCM in July 2013. He has assembled an executive editorial board with Prof. Peter Hylands of KCL and Prof. Jan van der Greef of University of Leiden. Prof. Kelvin Chan and Prof. Pierre Duez led the GP-TCM SOP team to produce a review Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on traditional Chinese medicine and Chinese materia medica in Journal of Ethnopharmacology.

Priority areas:
- Advance and emphasise global harmonization of regulation of complex herbal products in general and CHM in particular;
- Strengthen research agenda to employ functional genomic approach with all omics tools in connection with network systems pharmacology/toxicology;
- Engage the British Pharmacopoeia, the European Pharmacopoeia and the Chinese Pharmacopoeia in mutual recognition of a selection of medicinal herbs;
- Initiate dialogue with The WHO with respect to its place to co-ordinate a consultation process with the aim of putting forward suggestions for harmonisation to key regulatory agencies.

1.3.8 WP8 - Functional Genomics in Studies of Acupuncture-Moxibustion and Meridians

Objectives: The overall objective of WP8 was to optimise and standardise acupuncture protocols and discuss the application of the functional genomics approach and to examine the efficacy of acupuncture and moxibustion for the treatment of common diseases in the EU countries. The specific objective was to first establish a communication and collaboration platform to evaluate the current status of acupuncture research and practice in both China and EU. And then, define and prioritise research areas or topic in acupuncture that would be appropriate for conducting functional genomic studies. Another objective was to obtain general agreement on the common standards for acupuncture protocols. The most important objective was focusing on future research strategies within appropriate areas for functional genomics.

Description of work: The tasks for WP8 were focused on functional genomics studies in acupuncture and moxibustion. All activities relied on international collaborations and coordination.
Firstly an effective communication and collaboration platform needed to be established for the acupuncture-moxibustion research and practice in both China and EU. The Kick-off meeting of WP8 was held on schedule from 31st October to 1st November, 2009 in Beijing, China. During this meeting, members passed the final version of the WP work plan and agreed on most of the task-related issues and work assignments. WP8 homepage was developed and contributed to overall project website construction which was integrated with all WPs involved. Moreover, as web-based communications were important for the management of WP8 internal businesses, WP8 leads have developed well-organised communications with members of WP10, WP6 and WP8 by phone and email, to discuss the GP-TCM

issues. Regular teleconferences, email communications and face-to-face meetings were used to discuss WP8 problems. 36 teleconference meetings were held and the D8.4 was updated quarterly. In addition, a joint face-to-face meeting (with WP6) was held in Beijing, China on September 2011 to identify the key tasks for the final year of the project and topics for future research.

The first stage of WP8 focused on the joint survey of Chinese acupuncture practitioners in collaboration with WP6. A questionnaire was designed and carried out with TCM practitioners in China and the EU to ascertain their perceptions of clinical evidence for TCM and where future research should focus. TCM practitioners in the EU (in collaboration with 30 professional acupuncture and TCM organisations) and in China (from selected hospitals and institutions) were targeted. Data was added into a database and analysed. The acupuncture data was published in the GP-TCM Special Issue of the Journal of Ethnopharmacology in 2012.

The second stage focused on the "the functional genomics areas/aspects of acupuncture". A report focusing on the pitfalls and solutions for functional genomic studies in acupuncture has been finished. Literature reviews on prioritised research areas and future research strategies of acupuncture, appropriate for conducting functional genomic studies were performed and published in the GP-TCM special issue of Journal of Ethnopharmacology. The WP8 members also attended the 1st and 2nd Annual General meeting and the Final Conference and presented the work of the WP.

The expert panel of WP8 has been substantially improved and expanded and now includes 9 beneficiary and 22 non-beneficiary partners. All 8 deliverables of the WP were completed and the reports were submitted.

Outcomes:

The expert panel of WP8 has changed and expanded over the project period, but WP8 has maintained a close relationship among all WP members and with WP10. Several considerations were planned and carefully balanced during the entire team assembly processes, such as stability/dynamism, specialty/collaboration, broad coverage/representative subjects, and experienced seniors/young enthusiasts, etc. Based on the international collaborations and coordination, an extensive collaborative panel clinical and basic research in acupuncture was established both in China and EU. Activities such as a WP kick-off meeting, some other face-to-face meetings, literature studies, a number of teleconferences and many email communications were carried out in order to meet the WP objectives and milestones. The current status of clinical and basic research on acupuncture was highlighted to foster research collaboration both within and between China and the EU.

The results from the online survey identified differences in practice and training between acupuncturists in China and the EU and between EU member states and the data was published in the special issue. These differences may inform prioritisation of health conditions for future trials. Innovative research methods are recommended to incorporate the complexity and plurality of acupuncture practice and theory. Creation of collaborative networks is crucial in overcoming these differences to facilitate international, multi-centre clinical trials.
Literature reviews on prioritised research areas and future research strategies of acupuncture that are appropriate for conducting functional

genomic studies were performed and published in the special issue. Disease-oriented studies using the approach of multi-indexed high-throughput technologies and systems biology analyses will be a preferred strategy for future acupuncture/moxibustion research was also highlighted in report.

In addition, an article on the application of genomic technology in acupuncture treatment of Parkinson's disease has been published in Evidence-based Complementary and Alternative Medicine. An increasingly popular area for acupuncture is infertility. Taking this topic as an example a systematic review was carried out of the literature highlighting the areas needing attention, and which provided highlighted guidance and recommendations for future trial design in acupuncture. This article has been published in the Journal in the European Journal of Integrative medicine and referred to in the accompanying editorial of the journal.
Various publications disseminating the activities of WP6 has been published (Part 4.2A1 - List of SENTIFIC PUBLICATIONS).

Priority areas:
- The results from the online survey identified differences in practice and training between acupuncturists in China and the EU and between EU member states. It is suggested that creation of collaborative networks is crucial in overcoming these differences to facilitate international, multi-centre clinical trials.
- WP8 has created a review of existing literature and suggested a preferred strategy for future acupuncture/moxibustion research. Focused on several diseases or symptoms with evidence of effectiveness by acupuncture treatment, the approach of combination Omic technologies with functional molecular imaging will be a preferred strategy for future acupuncture research.
- WP8 also defined the status of current Chinese clinical-related acupuncture basic research in order to highlight future inter-collaborative research between and within China and EU.

1.3.9 WP9 - Final Conference

Objectives: The task for WP9 was to organise and host the final conferences. This task was split up in two parts. One was the Final Conference, which was for project members to finalise the conclusions of their WPs; the other was for results to be presented in an international forum open to the public, i.e. the GP-TCM Congress. The deliverable D9.2 reports the full details of the organisation and results of both meetings.

Description of work: From the very beginning of the project, the local organizers in Leiden have been exploring various sites for the Final Conference. They visited several facilities and eventually have chosen for the congress centre in Rolduc, an old monastery which can easily be reached by train from both Germany and the Netherlands. The Rolduc meeting attracted 80 participants. It was also decided with the management committee that besides the internal symposium for the beneficiary and non-beneficiary members of the project, WP9 also should organise a second meeting to disseminate the results to the scientific community. For that symposium, the facilities at the Leiden University were chosen. The program for the final project meeting, i.e. the Final Conference, was used to finalise the reports of all the work packages. The work package leaders were invited as speakers for the meeting in

Leiden, together with some further invited speakers. Also there was the possibility for short oral presentations and posters in the open meeting, i.e., the GP-TCM Congress. The program in Leiden thus attracted 130 participants. There were 15 plenary lectures, 18 short presentations and 37 posters. Also there was a workshop in which the Dutch Society against Quackery gave their view on the problems with TCM, followed by a presentation about the objectives of the meeting, and ended with an open discussion on the demands on research to come to evidence-based medicines.

For the organisation of all the practical part of the meetings, advertisement, website, general correspondence with participants, finances, extensive correspondence and phone calls about visa, registration, catering, accommodation of speakers, book keeping of costs and income, etc. two externals with experience of organising international scientific meetings were hired from the budget. Via the regular teleconferences and by presenting the plans at the previous meetings, the consortium was able to reach out to many people all over the world.

One of the important deliverables of WP9 was to disseminate widely the conclusions from the conference through printed proceedings that is: 'Organising peer review of conference proceedings and submitting for publication in open access scientific journals'.

Therefore, after intense and fruitful discussions, the consortium decided to reach out most efficiently by publishing the results of the project in a special issue of Journal of Ethnopharmacology (Impact Factor: 3.014, in the top 20 of more than 2000 Elsevier journals with most full text downloads). This special issue is an important step towards defining rules for the "Good Practices" in our research, and setting standards for evidence-based traditional medicines. To achieve this, the consortium has been negotiating with Elsevier and also discussed extensively with WHO representatives about the best way to reach out with the results of the project. Elsevier was willing to make a special deal that allows the special issues to be freely accessible (open access) thus reaching out till anyone interested to read the outcome of the project. The special issue was edited by Dr. Qihe Xu and Prof. Rudolf Bauer. It contains 20 peer-reviewed publications covering all the aspects as discussed in the past years in the project. The issue counts 188 pages and was the issue 3, volume 140 of the Journal of Ethnopharmacology, 2012.

Besides this, also the abstracts of the Leiden meeting have been collected and are available on a USB-stick together with the complete contents of Journal of Ethnopharmacology issue.
To disseminate the results to the general public, WP9 and other WPs supported reportage for the News on several Television channels in the UK and China.
Outcomes: The major outcomes of the WP9 were the two meetings. One with about 80 participants was to finalise the conclusions of consortium and its 10 WPs in Rolduc, the Netherlands; the second, with about 130 participants in Leiden, the Netherlands, was to disseminate the results of the WPs to the scientific community. We were able to give 15 students a grant for the Leiden meeting to help cover their registration costs. Otherwise, WP9 followed the COST rules for travel costs (see http://www.cost.eu/participate/guidelines online). The costs for the Rolduc accommodation and food were calculated and based on that the registration fee for each participant was calculated, and given as a

grant to each of them, the grant money was used to pay to the congress centre. Besides these meetings, a special issue of Journal of Ethnopharmacology was published with the contributions of the different work packages. This issue is open access. Also all participants in the meetings obtained an USB stick with the whole issue stored. For dissemination of the results to the public, a television maker made a series of reports, which were broadcast in Pheonix TV in both Europe and China.

http://project.GP-TCM.org/2012/05/GP-TCM-meetings-on-tv/

It was a great experience to have the opportunity to organise these meetings, though we had experience of 20 years organising international meetings almost every year, these meeting were much more labour-intensive, because normally participants come and pay a registration fee, and as organiser one carries only responsibility for the invited speakers. For the Final Conference, as organizers we were responsible for all the guests. Majority of the participants were beneficiary members, where all participants were reimbursed under the same financial rule set by the WP9 Coordination. At the same time, WP9 did their best to ensure all non-beneficiary members, who attended the meeting had their expenses reimbursed within the available budget. These arrangements as well as the problems in getting visas for non-European participants have taken an enormous amount of time.

All participants were asked to complete a questionnaire about all aspects of the meetings. Assessing the answers provided by the attendees, we have the impression that we managed to really satisfy all participants, as the scores of the survey were very good.

Priority areas:
- Networking will be a key aspect of further integration of the research;
- To have a COST project on TCM research;
- GP-TCM Research Association should organise postdoctoral courses on systems approaches to TCM research;
- EU and China should come to a mutual agreement to support studies on the integration of Chinese and European medicine;
- Dissemination of results to the general public.

1.3.10 WP10 - Management: Sustainable development and coordination of TCM research in the EU

Objectives: As the overall management team of the consortium, WP10 aimed to coordinate WP leadership, membership and collaboration, to steer research direction, to organise quality assurance, collation and integration of data, as well as dissemination of results.
Description of work: In 3.5 years, WP10 organised more than 50 major teleconferences covering management, science and good practice issues, 3 face-to-face consortium-wide meetings with relevant stakeholders' involvement, and numerous other face-to-face meetings to facilitate effective and efficient communication platforms and discussion fora moving the project forward.

The GP-TCM network focused on assessing the existing new technologies (i.e., omics) to help explain and understand TCM, especially on defining the good practices to generate reliable and reproducible data for registration of Chinese herbal products. There was a clear consensus on the need for evidence-based medicine endorsed by all consortium members.

While providing scientific leadership to all WPs trough number of specialised committees such as the e-MSM (online Management and Science Meetings) Committee, Advisory Board, Literature Review Panel, WP10 also provided platforms to establish commonly agreed best practice, priorities for future direction of research, and future activity across the consortium.

Outcomes:

- Ever-strengthening interdisciplinary, intersectoral and interregional collaborative network: By the 3rd year of the project, the consortium membership profile was increased from "28 beneficiary and 24 non-beneficiary partners across 12 countries" to "29 beneficiary and 82 non-beneficiary partners across 24 countries" giving access to further expertise and resources while strengthening the delivery of project objectives.

- Consortium-wide conclusions on grand Issues in TCM research: WP10 broke barriers among WPs and between GP-TCM and the other related communities and organised the GP-TCM "Grand Issues in Traditional Chinese Medicine Research Survey" open to all consortium members and non-members. The outcomes of the survey established high-quality research on efficacy/effectiveness and mechanisms of action of CHM and acupuncture and identification of priority disease areas where TCM could achieve better outcomes as grand priorities. TCM contribution to the management of one of EU's top healthcare challenges, i.e. long-term conditions and chronic diseases was regarded as the top opportunity.
Results of the poll were made freely available through the following web links:
http://project.GP-TCM.org/2011/08/"grand-priorities-challenges-and-opportunities"-survey/
http://www.sciencedirect.com/science/article/pii/S0378874112001110

- The open-access GP-TCM Journal of Ethnopharmaology special issue: WP10 played a key role in disseminating the project findings. To summarise the research outcomes and recommendations from all GP-TCM WPs in a way convenient for future reference, the consortium prepared a series of publications derived from the GP-TCM consortium to be collated into a special issue of the Journal of Ethnopharmacology. The special issue was published in April 2012 and comprised 20 articles, with contributions from all WPs as well as independent papers complementary to the work of GP-TCM. The consortium made all articles open-access, allowing all interested parties to download the articles free of charge
http://www.sciencedirect.com/science/journal/03788741/140

- Three WP10 contributions to the above special issue, among many more other dissemination papers:
 - Good practice guidelines on reviewing and publishing studies of herbal medicines, especially CHM:
http://www.sciencedirect.com/science/article/pii/S0378874112000517
 - TCM research in the post-genomic era: Good practice, priorities, challenges and opportunities:
http://www.sciencedirect.com/science/article/pii/S0378874112001110
 - Good Practices: The basis for evidence-based medicines:
http://www.sciencedirect.com/science/article/pii/S0378874112001183

- The GP-TCM Research Association: GP-TCM good practice guidelines need dissemination, validation and further development through continued

interregional, interdisciplinary and intersectoral collaborations. Hence to promote this, WP10 led the process of establishing a new international association, known as "the GP-TCM Research Association", which was founded in April 2012 and has fully succeeded the 3.5-year fixed-term FP7 GP-TCM consortium since November 2012 (see http://www.GP-TCM.org/ online).

- Members' answers to the question "What have I learnt through the GP-TCM project?": To mention a few, Prof. PC Leung (Chinese University of Hong Kong, China) said: "GP-TCM has demonstrated the potential of collaboration in the vast field of TCM; GP-TCM should be continued." Prof. Olavi Pelkonen (University of Oulu, Finland) acclaimed: "Networking of scientists with variable backgrounds is powerful!" Prof. Rob Verpoorte (Leiden University, The Netherlands) conlcuded: "GP-TCM has lowered barriers between scientists from the EU and China, the GP-TCM Research Association will be instrumental in further lowering these barriers."

- Dissemination of findings to academia, industry, regulators and funders and the public: As detailed in Part 2 of this report (4.2A2) and the Deliverable D10.9 report.
Difficulties and solutions:

- As part of the financial difficulties of UMINHO, Portugal, some attendees of the 2nd GP-TCM AGM could not be reimbursed of their travel costs by the host institution UMINHO. KCL made the use of its budget for unforeseeable costs and had all the outstanding claims sorted to ensure that the reputations of the EU and the FP7 GP-TCM consortium were un-affected.

- All 10 WPs underwent significant membership changes and 6 WPs had significant WP leadership changes. These membership and leadership changes might cause temporary difficulties in coordination, but they served very well to ensure that each WP had all the needed human resources, expertise and vigorous leadership and eventually a success.

- Language barriers and lack of reliable and sustainable databases and literature resources in English remain key barriers for European scientists to get access to TCM literature. This was partially solved through recruiting scientists who are competent in both Chinese and English.

Overall conclusions and recommendations:

Due to its personalised and function-oriented features and its holistic and pre-emptive approaches, TCM is highly complementary to the current model of Western medicine and thus represents an important field for future research. Looking forward, prospects for the whole area largely depend on how experts in different disciplines and stakeholders in different regions and sectors collaborate and how much funding is invested into this field.

To reach the goals of better quality, safety and efficacy, the GP-TCM consortium propose that the rules of integrity (good practice), integration (collaboration) and innovation must be followed in the future of TCM research.

Priorities:

- Sustainable governmental and non-governmental funding in this promising area, e.g. supporting EU-China joint initiatives on TCM research and development, supporting training programmes on good practices in TCM research, etc;
- Interregional, intersectoral and interdisciplinary collaborations in quality control, pharmacovigilance, toxicology and pharmacology of CHMs and high-quality clinical trials;
- Special focus on research of TCM interventions, including prevention and treatment, for chronic diseases.

Potential Impact:

4.1.4 The potential impact and the main dissemination activities and exploitation of results:

GP-TCM played a keen role to have a durable impact on European focused TCM research. All its major activities including development of sustainable expert networks, generation of guidelines, reviews, recommendations and priorities, as well as development of online resources and establishment of the new TCM research association were designed to have maximum impact on development of European agenda for future research and funding, as well as policy making. In addition, through series of open-access reports, peer reviewed articles, and public dissemination events, the consortium maximised its engagement with public and other key audiences within and beyond Europe.

1.4.1 Impact through Developing a Large Interactive and Collaborative Expert Network:

GP-TCM was characterised as an open-start and open-ending consortium. With the launch of the consortium in May 2009, scientists in Europe and China, who had been working on TCM research independently, were gathered under the project's banner and their efforts were unified to reach consensus on good practice guidelines, state-of-the-art functional genomics, as well as grand priorities, challenges and opportunities in studies of TCM.

To effectively address the issues dealt with by the project and to drive forward TCM research using a functional genomics strategy and coordinate country actions, the initial European-Chinese network evolved into an international team of experts working as a large collaborative super-network involving approximately 200 scientists from 110 institutions across 24 countries, while a clear EU-China focus remained. Such a large and dynamic collaboration gave the consortium the privilege to get access to stakeholders around the world, as well as broader, deeper and more authoritative expert knowledge and resources. This helped the consortium develop globally competitive comprehensive good practice guidelines, handbooks and reports, including those on scientific reporting of TCM studies, clinical trials and the applications of omics technologies in various aspects of TCM research.

Involvement of partners and stakeholders was further supported by providing discussion platforms including more than 20 face-to-face meetings, more than 50 teleconferences, intranet, newsletters, BBS fora and numerous e-mail exchanges, in which all major aspects of CHM and acupuncture studies were covered. These platforms greatly facilitated effective communications among experts from universities, hospitals, industry and governments, as well as from other public and private sectors, and facilitated the delivery of one of the project's primary objectives to inform the best practice and to harmonise research into TCM through interregional, interdisciplinary and intersectoral collaboration.

The links generated between partner institutions and scientists thorough the project also led to lasting partnerships and further collaborations. A number of joint proposals have already been awarded EU and Chinese grants and many more collaborations targeting international and national grants will be explored in the coming years.

1.4.2 Impact through Novel Literature Research Findings and Recommendations of 10 WPs:

During the lifetime of the project, the consortium reviewed existing TCM literature and other data to assess the state-of-the art omic technologies and their use in evidencing safety, efficacy and mechanisms of action of TCM. These reviews and peer discussions allowed our scientists to identify knowledge gaps and provide standardised methodologies and good practice guidelines in relevant TCM research fields. Their studies especially focused on challenging areas, which will have impact on health of EU citizens.

The findings and conclusions of the consortium WPs have been presented in the forms of reports, guidelines, handbooks, peer-reviewed scientific articles, web posts, newsletters, posters, talks, etc. The material produced by the consortium has been tailored to serve the needs of the public as well as the expert community (science, policy making and funders).

Contributions by each WP to advance TCM research in Europe are summarised below:

WP1 (Quality Control):
- Compiling a "priority list of species" of particular importance for the EU;
- Report showing the different scientific names that can be assigned to the species used in a classical CHM formula Liu Wei Di Huang Wan.
- Information about the methods used to prepare the species used in Liu Wei Di Huang Wan as well as information about institutes that contain verified vouchers for these species.
- Review article: Good practice guidelines in reviewing and publishing studies on herbal medicine, with special emphasis on Traditional Chinese Medicine and Chinese Materia Medica. J Ethnopharmacol. 2012; 140: 469-475.
- Review article: The formation of Daodi Chinese materia medica. J Ethnopharmacol. 2012; 140: 476-481.

WP2 (Extraction and Component Analysis):
- Report summarising techniques and standards employed for the analysis of simple and complex herbal extracts;
- Report summarising techniques and standards employed for the preparation of extracts used in TCM;
- Report on best practice in information analysis for fingerprinting and component analysis;
- Report on the methodology used in the analysis of 'priority list preparations';
- Report on identified gaps of information and non-standard areas;
- Recommendations for future research agenda;
- Review article: The potential of metabolic fingerprinting as a tool for the modernisation of TCM preparations. J Ethnopharmacol; 2012; 140: 482-491.

WP3 (Toxicology):
- Establishing the definition to "toxicity" as "possible harmful reaction to the body which is not related to therapeutic effect;
- Classification of "toxicity" into four major groups: (i) side effects (covered by pharmacodynamics and often predictable), (ii) reactions occurirng as a result of overdose, overduration, tolerance, dependence-

addiction (covered either by pharmacodynamics and pharmacovigilance), (iii) hypersensitivity, allergic and idiosyncratic reaction (covered by pharmacovigilance), (iv) mid-term and long-term toxic effects (liver, renal, genotoxicity, teratogenecity, neurotoxicity, cardiotoxicity, etc);
- Consensus on (iv) mid-term and long-term toxic effects as the most important field for omics predictive toxicology;
- Review article: Review of current and omics methods for assessing the toxicity (genotoxicity, teratogenicity and nephrotoxicity) of herbal medicines and mushrooms. J Ethnopharmacol; 2012; 140:492–512.
- Review article: Pharmacovigilance practice and risk control of TCM in China. J Ethnopharmacol; 2012; 140: 519–525.
- Review article: Pharmacovigilance of herbal medicines. J Ethnopharmacol; 2012; 140: 513–518.
- GP-TCM collaboration led to new projects entitled "Neuro-biological mechanism of KXS on memory enhancement" and "Research of effective components from Polygala tenuifolia on improving learning and memory in vivo", which have been funded by MOST, China.

WP4 (In-vitro and In-silico Pharmacology):
- Evaluation criteria for scoring scientific articles on CHM research articles, which can be used to evaluate the quality of the scientific reporting; freely available to the scientific community for scoring scientific papers in the field;
- An online repository of literature encompassing in-vitro research and functional genomic applications of CHM, which is available to the scientific community and can be used to understand the weighed quality of papers on specific CHM subjects;
- Report of the discussion group on biological target oriented database, which is available to the public on the GP-TCM project website and can stimulate scientific debate;
- Report on quality criteria and scoring of the CHM database, which is available to the public on the GP-TCM project website and can stimulate scientific debate;
- Report on existing databases and software for in-silico studies of phytocomplexes, which is available to the public on the GP-TCM project website and can stimulate scientific debate;
- Handbook on good practice in the reporting of CHM experimental work, which is available to the scientific community on the GP-TCM project website and suggests good practices for scientific reporting in in-vitro CHM research;
- Handbook of guidelines for using in-silico tools in CHM research, which is available to the scientific community on the GP-TCM project website and suggests good practices for using databases and software in in-silico CHM research;
- Handbook for using functional genomics techniques in in-vitro CHM research, which is available to the scientific community on the GP-TCM project website;
- A questionnaire survey on scientists' views regarding the value of the application of omic and in-silico methods in TCM research, which is available to the scientific community on the GP-TCM project website and can be shared by the scientific community to repeat the analytical test in different contexts;
- A searchable online repository of critically reviewed and quality scored articles, which is available to the scientific community on the GP-TCM project website and can be used for reviewing purposes by the scientific community;

- Review article: Omic techniques in systems biology approaches to traditional Chinese medicine research: Present and future. J Ethnopharmacol. 2012; 140: 535-544;
- Review article: In-silico studies in Chinese herbal medicines' research: Evaluation of in-silico methodologies and phytochemical data sources, and a review of research to date. J Ethnopharmacol. 2012; 140: 526-534.

WP5 (In-vivo Pharmacology):
- Review article: MEDLINE-based assessment of animal studies on Chinese herbal medicine. J Ethnopharmacol. 2012; 140: 545-549.
- This review on CHM literature involving animal models resulting in the identification of the main problems in the experimental design of animal studies of CHM and the assessment of the scientific proof of the efficacy of CHM provided by animal studies. This can be used for the scientific community;
- Provision of a checklist that could help in the preliminary selection of publications lacking the most common problems of animal studies of CHM and thus would be useful for a quick search of reproducible CHM treatments that are likely to be effective in a given context. The second application of this checklist is to help avoid the most common problems when designing experiments. Therefore the checklist provides guidelines for the good practice in the conduct of CHM studies in animals and it is recommended for use by researchers. This will ensure a solid evidence base for the efficacy of CHM and for the use of more holistic approaches based upon the application of omic technologies.
- Review article: Omic techniques in systems biology approaches to traditional Chinese medicine research: Present and future. J Ethnopharmacol. 2012; 140: 535-544.
- This WP4 and WP5 joint review highlighted the application of omics and systems biology technologies in both in-vitro and in-vivo studies of TCM and can be used as a state-of-the-art report on this important issue;

WP6 (Clinical Studies):
- Provision of clinical research good practice guidelines for CHM trials. These will be recommended for use by researchers and the academic community. This will in the future ensure the provision of a solid evidence base for policy and clinical CHM use.
- Report on clinical use of CHM, specifically comparing the clinical use of different kinds of preparations of CHM. This and future research in this area will impact on good clinical practice and improve patient care.
- Report on the role of Omic technologies for CHM highlighting the general scope where future research may prove useful. This underpins the need for good practice and highlighted the importance of defining quality standards for CHM products, toxicity, differentiating the actions of single and multi-component CHM mixtures and drug responses. This is of key importance to clinicians, researchers, the pharmaceutical industry and policy makers.
- Identification of areas of clinical importance to and evidence gaps in clinical practice by engaging with TCM practitioners and Western conventional practitioners. This may have impact on integration of TCM and conventional medicine.
- Review article: Comparison of effectiveness and safety between granules and decoction of Chinese herbal medicine: A systematic review of randomized clinical trials. J Ethnopharmacol. 2012; 140: 555-567.
- Review article: Guidelines for randomised controlled trials investigating Chinese herbal medicine. J Ethnopharmacol. 2012; 140: 550-554.

WP7 (Commercial R&D and Regulatory Issues):
- A comprehensive paper providing comparisons of the different regulatory pathways for CHM products and other traditional herbal medicines including tabular comparisons and flow diagrams;
- A comprehensive analysis of omic technology being used for R&D of pharmaceuticals and how this can be applied to the future R&D of CHMs;
- An extensive collaborative international network of experts in CHM R&D and in particular, the applicable regulations and omic technology. Experts representing a good cross section of the life sciences i.e. academia, industry, government;
- Dialogue with key regulatory agencies and inclusion of Agency staff in WP7 membership.
- Review article: Future development of global regulations of Chinese herbal products. J Ethnopharmacol. 2012; 140: 568-586.
- Review article: Omics and its potential impact on R&D and regulation of complex herbal products. J Ethnopharmacol. 2012; 140: 587-593.

WP8 (Acupuncture and Moxibustion Studies):
- An effective collaborative international network of experts in acupuncture research has been identified for future clinical trial research;
- WP8 and WP6 launched an acupuncture and TCM practitioner survey across Europe and China. The survey (WP8 part) explored the acupuncture practitioners to identify the most common conditions treated by acupuncturists and compare the different conditions treated by acupuncture practitioners in China and EU. Their views on effectiveness were ascertained in order to identify areas where clinical trials on acupuncture should focus. This is of use to clinicians, government, researchers and academics in defining the topics for future clinical trials and the current evidence gaps;
- Literature reviews suggested that disease-oriented studies using the approach of multi-indexed high-throughput technologies and systems biology analyses could be a preferred strategy for future acupuncture/moxibustion research. This will be of use to all stakeholders in acupuncture research.
- Review article: A review of Omics research in acupuncture: The relevance and future prospects for understanding the nature of meridians and acupoints. J Ethnopharmacol. 2012; 140: 594-603.
- Review article: Exploring practice characteristics and research priorities of practitioners of traditional acupuncture in China and the EU-A survey. J Ethnopharmacol. 2012; 140: 604-613.

WP9 (Final Conferences):
- Through advertising the Leiden meeting we reached many colleagues in the field, resulting in new members of the network.
- The GP-TCM Journal of Ethnopharmacology Special Issue [2012; 140(3)] was freely distributed and promoted at the two WP9 meetings; it will sets standards for research on traditional medicines for a number of years to come.
- The GP-TCM Association was initiated at one of the two meetings organised by WP9.
- Identification of future stakeholders that expressed their interests in the Association through the survey spread to all participants.
- Dissemination of results to a large scientific community.
- Review article: Good Practices: The basis for evidence-based medicines. J Ethnopharmacol. 2012; 140: 455-457.

WP10 (Management):
- Identified a future research agenda for Europe and beyond through the GP-TCM survey entitled "Grand Issues in TCM Research", focusing on grand priorities, challenges and opportunities". This document will serve as a major guideline to help shape the future research focus and funding opportunities by funders, policy makers and TCM scientists'.
- Organised the publication of an open-access GP-TCM Journal of Ethnopharmacology Special Issue to provide all-in-one reference document summarising project's focus areas, literature reviews, findings and recommendations.
- The GP-TCM Research Association was founded to sustain coordination of good practice in TCM research in the EU and a stronger alliance with the other parts of the world.
- Review article: Establishing an EU-China consortium on traditional Chinese medicine research. Chin Med. 2010; 5: 42.
- Review article: Traditional Chinese medicine research in the post-genomic era: Good practice, priorities, challenges and opportunities. J Ethnopharmacol. 2012; 140: 458-468.
- Review article: Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on traditional Chinese medicine and Chinese materia medica. J Ethnopharmacol. 2012; 140: 469-475.
- Review article: Network pharmacology and TCM. In: Alternative Medicine. Sakagami H, ed. Intech, ISBN 978-953-51-0903-7. This is an in-press Intech open-access book chapter, which introduced the concept of network pharmacology, TCM network pharmacology and their applications in TCM research.
- Review article: "The role of the GP-TCM Research Association to modernization and globalization of Traditional Chinese Medicine" in the book "Antitumor Potential and other Emerging Medicinal Properties of Natural Compounds" to be published by Springer.
- Review article: The quest for modernisation of TCM. Submitted to an open-access journal BMC Medicine. This manuscript reviewed the concept and practice of the "modernisation of TCM" in an international, historic and scientific perspective, leading to the three "I" principles below.

1.4.3 Impact through Developing the Three "I" Principle:

The consortium has recommended three "I"s to guide future development of TCM research, i.e. integrity, integration and innovation, which are interpreted as follows.

- Integrity
- Holism. As a holistic medicine, TCM considers the human body as a whole, emphasises the importance of functions and emotions and considers patients as part of a system interacting with its environmental factors, such as diet, climate and life style. This is embodied in TCM diagnosis, prescriptions and life style interventions.
- Ethics. Since the era of Sun Simiao (581-682) ethics has become an integral part of TCM. In ancient China, practitioners' ethics were at the centre of the TCM profession. Now, modern TCM ethics should apply to not only TCM practitioners, but also the agricultural, industrial and scientific communities, and all stakeholders. Conflict of interests should be avoided, stated and properly regulated.
- Good practice. As defined by the FP7 GP-TCM project and the GP-TCM Research Association, TCM requires continuous development, refinement and dissemination of good practice guidelines in all its multiple aspects. In such epic efforts, collaboration and sharing must be encouraged and we must strive for consensus while respecting differences. Good practice is

especially required in authentication, quality control, safety assessments and sustainable use of TCM drugs and materials; agricultural and manufacturing practices; commercial and clinical practices; clinical and basic research of TCM; application of routine and emerging technologies; as well as differentiation between valuable knowledge and superstitious, erroneous and misleading anecdotes.

- Integration

- Education, clinical practice and research. Integration of these three important aspects was one of the most important achievements in modernisation of TCM.
- Cultural, philosophical and scientific perspectives. TCM is an important part of Chinese culture and is guided by Chinese philosophy. Thus, researchers of the scientific, cultural and philosophical values of TCM should collaborate with and learn from each other.
- TCM, Western medicine and modern science. In China and some other countries, TCM and Western medicine are both in mainstream healthcare and intend to complement each other. In the international context, dialogue between TCM and Western medicine needs to be promoted; China's experiences and lessons should be studied in light of modern science so that both medical traditions may contribute to forging tomorrow's medicine. Bringing evidence-based medicine to recognise the value of TCM will have to integrate a thorough rethinking of both Western and TCM practices to generate scientifically and statistically convincing evidence of the TCM-based approaches.
- Interregional, intersectoral and interdisciplinary collaborations. Due to the complexity and the vast range of TCM, collaborations between different regions, different business sectors, as well as different areas of knowledge must be encouraged in order to share resources and expertise and join forces to meet the challenges together. For example, the various distribution channels encountered in different countries must be connected in order to develop harmonised pharmacovigilance procedures suitable to rapidly and globally detect and assess warning signals for adverse events.
- Holistic, relationist and analytical, reductionist approaches. TCM emphasises holistic and relationist approaches of thinking, while Western medicine is largely based on analytical and reductionist approaches. To see both the trees and the wood, these approaches must be integrated.
- Quality, toxicology and pharmacology. These three most important aspects of TCM are so much interrelated that future training and research must further integrate these crucial elements to better ensure safety and efficacy.

- Innovation

- Modernisation of TCM is more than Westernisation. Although some achievements have already arisen through studying TCM using a Western approach, e.g. isolating pure compounds, real innovations should include both TCM-inspired changes in mode of thinking and practice in Western medicine and TCM refinements inspired by modern science.
- TCM diagnosis. Among all aspects of TCM, holistic TCM diagnosis has probably the most complementary elements to modern medical practice, including its function-oriented description of organ systems and diagnostic approach (leading to syndrome differentiation), its emphasis on modulation of functional balance, its comprehensive categorisation and interpretation of tongue and pulse patterns, its characteristic categorisation of the nature of diseases and drugs, etc. These could be important sources for developing and validating innovative mind-set,

methods, tools and strategies that could complement biology-based diagnosis.
- Preventive and comprehensive interventions. TCM is characterised by both pre-emptive approaches and interventions with multiple components. It emphasises intervention before disease arises and often combines dietary advice, physical exercises such as Taijiquan (Tai Chi Chuan), meditation, herbal medicines, massage, acupuncture and moxibustion, etc. The values of these individualised and integrated approaches are important directions for future public health.
- Innovative, more robust methodology. The complexity of TCM demands novel and more robust ways of thinking, approaches, tools and methods. For example, the individualised and holistic nature of TCM requires tools for complexity research, research of the science of individuality and personalised medicine, as well as novel statistics. It also awaits the maturation of omics, systems biology and other systems-based technologies.
- Prioritisation and focus. In view of the vast areas of TCM yet to be explored and the limited resources available for such an emerging area of research in the global context, prioritisation and focus become the key to achieving real innovation. In this regard, a Steve Jobs approach for innovation is to "say no to 1,000 things" and to focus only on those that could make real differences becomes all the more compelling.

1.4.4 Impact through Developing Online Resources:

The consortium developed numerous reports, peer-reviewed articles, guidelines, databases and newsletters to support best practice, exchange of experience and strengthen EU focussed international collaboration in TCM research. These resources were made available online through various sources open to members or to the public. It is envisaged that these online resources will continue to support and enhance Pan-European studies of TCM research while being used as references by policy makers and funders.

- The GP-TCM project (archived) and the GP-TCM Research Association websites: The project website will be kept online for at least three years after completion of the project's funded lifetime to allow continuous access to our outcomes by the public.
http://project.GP-TCM.org; http://www.GP-TCM.org/
- The GP-TCM public deliverable reports ranging from technical reports, databases, guidelines to meeting proceedings – open access (74 documents)
http://project.GP-TCM.org/about/deliverables/
- The GP-TCM internal deliverable reports – members only (100 documents)
- The GP-TCM Special Issue – open access (20 review articles)
http://www.sciencedirect.com/science/journal/03788741/140
- The GP-TCM Newsletters – open access (54 issues published between October 2007 and October 2012): http://www.GP-TCM.org/news/
- GP-TCM Guidelines for randomised controlled trials investigating CHM
http://www.GP-TCM.org/2012/12/GP-TCM-guidelines-for-randomized-controlled-trials-investigating-chinese-herbal-medicine-chm-2/

1.4.5. Impact through Founding a New Association:

With the exception of the GP-TCM consortium, there was no pan-European organisation to coordinate TCM research in Europe. Hence, the consortium established a new organisation to carry on coordinating TCM research after completion of the project and ensure a sustainable development of TCM research in Europe and worldwide. The GP-TCM Research Association was

officially at a dissemination event organised by WP9 of the GP-TCM project, i.e. the GP-TCM Congress held in Leiden, the Netherlands, 16th – 18th April 2012.
The Association is a non-for-profit organisation, which is currently in the process to be registered as a charity in the UK. It will be dedicated to promoting high-quality evidence-based research of TCM through developing, disseminating and implementing good practice. The objectives for which the Association was established are:
- Perpetuate the interactive network established by the FP7 GP-TCM consortium;
- Promote discussion and implementation of good practice in TCM research and development, including the use of sustainably sourced materials;
- Advocate high-quality evidence-based research and development on TCM as well as on its integration with conventional medicine;
- Organise and co-organise scientific meetings and specialist courses;
- Nurture young TCM researchers at different levels in an interdisciplinary approach, including BSc, MSc, PhD and post-doctoral programmes;
- Facilitate collaborations and sharing of resources, expertise and good practice among members, industry and regulatory agencies;
- Encourage collaborations with existing relevant societies, consortia and organisations;
- Strengthen interdisciplinary, interregional, and intersectoral collaborations in TCM research and development;
- Perpetuate good practice in publishing TCM research outcomes;
- Disseminate scientific research outcomes and latest developments in regulatory sciences to stakeholders, industry, professional groups and the public.

1.4.6. Impact through Dissemination Activities:

GP-TCM was keen to disseminate findings on good practice issues and other important findings on the safety, efficacy and mechanisms of CHM and acupuncture to stakeholders and the public. Through agreed best practice, guidance and dissemination, the consortium aimed to harmonise activity to adhere to highest principles of scientific rigor within this complex field.

To achieve the consortium's dissemination goals, the following main activities were undertaken to inform the findings of the network to the widest possible audience including scientific community, industry, policy makers and the public:

- GP-TCM website and monthly newsletters;
- Consortium publications such as deliverable reports (public), periodic reports, a journal special issue and many other papers in scientific journals and books;
- Seminars, talks, workshops, demonstrations, interview reports by radio, TV, newspaper, specialist magazines and websites aimed at spreading the accruing research and review results to large communities;
- The Sino-EU GP-TCM Workshop (The GP-TCM Kick-off meeting, Beijing, China, 2009), Annual Meetings (Henley, UK, 2010; Braga, Portugal, 2011), the Final Conference and the GP-TCM Congress (Kerkrade and Leiden, the Netherlands, 2012); the 2012 Shanghai International Conference on TCM and Natural Medicine and the GP-TCM Research Association First Annual Meeting (Shanghai, China, 2012); and the International Symposium on Standardisation and Cooperation of TCM (Beijing, China, 2012);

- Establishment of the GP-TCM Research Association to sustain coordinated TCM research in Europe. Since its official launching in April 2012, the Association has joined forces with the GP-TCM project in dissemination efforts.

For example, the archived GP-TCM project website (see http://project.GP-TCM.org online) was one of the consortium's main tools for dissemination and communication internally and externally. The project website was regularly updated to provide freely downloadable resources such as reports, articles, databases etc. The GP-TCM newsletter was published on a monthly basis, and made available to be downloaded via the project website. The newsletters included information about consortium activities, membership changes, recommended reading, funding opportunities, etc.

Before the 2nd Annual general meeting (AGM) of the consortium, which was held on 22nd – 24th July 2011 in Braga, Portugal, a 1-day public dissemination conference entitled "Traditional Chinese Medicine Symposium" was organised and held by GP-TCM (21st July 2011). The event comprised talks from distinguished speakers covering from basic to state-of-the art TCM research, poster exhibition, and open debate on "TCM, phytomedicine and conventional medicine: How and where can they meet?". The event provided an excellent opportunity to introduce the project to new stakeholders from Europe and China as well as to inform public and disseminate findings.

The consortium held their final meeting, known as "the Final Conference", in Kerkrade, the Netherlands on 12th -13th April 2012. The Final Conference gathered more than 70 participants including beneficiary members, distinguished and devoted consortium experts (i.e., non-beneficiary members), together with representatives from major stakeholders and funders to disseminate the work and findings of the project and discuss future directions and collaborations.

In addition, the public dissemination event "the GP-TCM Congress" took place in Leiden, the Netherlands on 16th – 18th April 2012. The main objective of the Congress was to disseminate the results of the project by bringing together the project partners, external stakeholders and public (more than 130 attendees). During the 1st day of the Congress, the official launch of the GP-TCM Research Association took place which was followed by an open Members Meeting of the Association, informing the participants about its missions, objectives, bylaws, special interest groups, future meetings and other activities, etc. All participants of the Final Conference and the Congress were provided with the electronic versions of the GP-TCM Special Issue articles.

Furthermore, the Consortium actively disseminated it's studies and findings through presentations and talks, and exhibiting posters in national and international conferences, seminars, and workshops such as the 10th and 11th CGCM Annual Meetings (August 2011 and 2012, China), 8th World Congress of Chinese Medicine (September 2011, UK), Association of Traditional Chinese Medicine and Acupuncture UK Annual Conference (November 2011, UK).

At the invitation of American Association for the Advancement of Science (AAAS) journal Science, a 48-page Special Issue on TCM will be published in July 2013, comprising high-quality articles on theories/hypothesis, 'omics, regulation, clinical evidence and R&D of TCM. To enhance the

global impact of these articles, they will be embedded in 3 consecutive issues of Science in July 2013, and then complied into a single volume. 10,000 free copies will be published for dissemination in international conferences. This will prove to be the next major milestone in the dissemination efforts of the GP-TCM consortium since the publication of the open-access GP-TCM Journal of Ethnopharmacology Special Issue in April 2012.

1.4.7 Impact through Exploitation of Results and Resources Assembled by the Project:

- Made the best use of the ever-expanding FP7 GP-TCM network collaborating on good practice of TCM to establish an international Association, the GP-TCM Research Association.
- Made the best use of the communication and dissemination tools such as GP-TCM project website, newsletters and Essential Manual to build the GP-TCM Research Association website and newsletters;
- Informing the outcomes of the GP-TCM "Grand Issues in TCM Research" survey to stakeholders in the EU and China to serve forging an EU agenda for future TCM research and to guide future funding;
- Made the best use of GP-TCM agreements on state of the art, definition of good practice, guidelines and principles, priorities, challenges and opportunities to develop scientific publications;
- One PhD thesis on CHM was completed as part of WP5 literature studies;
- Three rounds of bidding for Seventh Framework Programme (FP7) Marie Curie Initial Training Network funding were launched in 2009, 2010 and 2011, respectively, with the expertise pool of the GP-TCM project;
- GP-TCM partnership between University of Vienna and Chinese Academy of Sciences led to successful seventh Framework Programme (FP7) in 2012;
- GP-TCM partnership between Chinese Academy of Medical Sciences and European partners led to successful funding from the Chinese government in 2012;
- Collaborations in the GP-TCM project and the GP-TCM Research Association led to closer collaborations and partnerships between many members. To mention a few, (i) the sister centre relationship between Shanghai Research Centre for TCM Modernization, Shanghai Institute of Materia Medica, Chinese Academy of Sciences (China) and the Institute of Pharmaceutical Sciences, Department of Pharmacognosy, Karl-Franzens-University Graz (Austria) was established in 2012; (ii) a memorandum of understanding was signed between King's College London (UK) and Chengdu University of TCM (China) to jointly support research and teaching of integrative Chinese medicine; and (iii) a new partnership between China Academy of Chinese Medical Sciences (China) and The Norwegian University of Science and Technology (Norway).

List of Websites:

http://project.GP-TCM.org