Good Practice in Traditional Chinese Medicine Research in the Post-genomic Era

GP-TCM

223154

D7.7

Programme on R&D of CHM for the Final Conference and submission for publication

Document description	
Name of document	Programme on R&D of CHM for the Final Conference and submission for publication
Abstract	This document summarises all the WP7 activities presented at the GP-TCM Final Conference in Kerkrade, the Netherlands (12-13 April 2012), plus minutes of the presentation itself and discussion by attendees of the conference.
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1 INTRODUCTION

At the GP-TCM Final Conference in Kerkrade, the Netherlands (12-13 April 2012), five WP7 members (Professor Kelvin Chan, Dr. Tai-Ping Fan (TPF), Mrs. Greer Deal, Mr. Alan Koo and Emeritus Prof. (eProf.) Olavi Pelkonen) reported on what WP7 had achieved over the past 3 years by means of a series of PowerPoint presentations. In addition, TPF announced that as a legacy for GP-TCM, he has been invited by AAAS Science magazine to edit a special sponsored issue on TCM in December 2012. A very unexpected outcome is that TPF has been involved in discussions at the UK's House of Lords regarding the future registration of TCM which demonstrates their interest in the regulation of Chinese medicines. This was followed by active discussions with other attendees of the conference.

This document summarises all the WP7 activities presented plus minutes of the presentation and discussion.

2 WP7 PROGRAMME AT THE GP-TCM FINAL MEETING IN KERKRADE, THE NETHERLANDS (12-13 APRIL 2012)

WP7 Session (11:45-13:00, 13th April 2012):

Chair: Prof. Kelvin Chan

Minutes: Mr. Alan Koo, Mrs. Greer Deal

Presentation session (Delivered by Dr. Tai-Ping Fan and Prof. Olavi Pelkonen)

A brief introduction to the WP7 objectives

Objectives

- To establish a collaborative network (consortium) that discusses the problems and solutions in developing Chinese herbal medicines (CHM) as drugs that meet the market-entry standard and requirement of the European Union and China.
- Special emphasis will be given to application of emerging functional genomics technology in this specific area.

With the approval of the Coordinating Office, WP7 underwent extensive re-structuring over the first 18 months, as to clearly re-assess its objectives and recruit appropriate members to execute agreed action plans. There was an urgent need for a universal regulatory framework for complex herbal mixtures. Without such a framework in place, major research proposals involving both academia and industry cannot be put forward as their commercial impact would be undermined. WP7 members agreed that their priority should be to support the development of harmonised guidelines for the regulation of botanicals as follows:

Objective (1) – Regulations:

To establish a collaborative network towards formulating an easy-to-follow statement on the various regulatory frameworks for botanicals, emphasising the synergies and highlighting the differences, in order to contribute to the long-term goal of global harmonisation.

Objective (2) – Use of "Omics":

To review the use of "Omics" in the regulation of drugs and its implication on the R&D of complex herbal products (CHMs)

Main activities of WP7 include:

1. Discuss the problems and solutions in developing Chinese materia medica as proprietary Chinese herbal medicines that meet the market-entry standard
2. Emphasise application of emerging functional genomics technology in this specific area
3. Interface with regulatory agencies in the European Union (EMA = European Medicines Agency) and China (SFDA = State Food and Drug Administration)
4. Undertake analysis of the Guidelines applicable to herbal products in the United States (FDA = Food and Drug Administration) and equivalent guidelines in Australia (TGA = Therapeutic Goods Administration) and Canada (NHPD = Natural Health Products Directorate)
5. Consider and undertake analysis of the Guidelines applicable to herbal products in other countries: Africa, Brazil, Japan, Russia, South Korea and Taiwan.
6. Propose a method for reaching a global harmonised registration strategy
7. Search literature beyond herbal products and summarise what has been reported on the application of "omics" in regulation of any drugs and then discuss its implications on regulation of complex herbal products (CHP) and Chinese herbal medicine (CHM)

A brief history of WP7 membership and leadership development

- Since the award of the GP-TCM grant, there have been changes in WP7 leadership. The original Coordinator Dr. Eddie Bair and Deputy Coordinator Tom Neuman resigned and were replaced by Prof. Kelvin Chan and Dr. Tai-Ping Fan, respectively. In December 2009, Dr. Tai-Ping Fan became Co-Coordinator following Prof. Kelvin Chan's departure from Wolverhampton University for a new post in the University of Sydney.
- The WP7 membership underwent significant organic growth over the 3 year period bringing together a network of experts and specialists spanning many countries. In year three, WP7 membership consists of both beneficiary and non-beneficiary members from academia, regulatory agencies and industry. The membership is as follows (in alphabetical order):

Beneficiary members

Dr Anu Aaspõllu (Asper Biotech, Estonia)

Prof. Kelvin Chan (WP7 Co-Coordinator, University of Sydney & University of Western Sydney, Australia)

Dr. Tai-Ping Fan (WP7 Co-Coordinator, University of Cambridge, UK)

Prof. Peter Hylands (King's College London, UK)

Prof. Werner Knöss (Federal Institute for Drugs and Medical Devices, Germany)

Prof. Chenghai Liu (Shanghai University of Traditional Chinese Medicine, China)

Dr. Qihe Xu (King's College London, UK)

Non-beneficiary members

Prof. David Briggs (University of Western Sydney, Australia)

Dr. Abraham Chan (PuraPharm, China)

Prof. Yuan Shiun Chang (China Medical University, Taiwan)

Dr. Shaw Chen (US FDA)

Mr. Bobby Deal (Global Regulatory Services, UK)

Mrs. Greer Deal (WP7 Deputy Coordinator, Global Regulatory Services, UK)

Dr Jin-Hui Dou (US FDA)

Dr. Svetlana Ignatova (Brunel University, UK)

Prof. William Jia (University of British Columbia, Canada)

Mr. Alan Hoi Lun Koo (WP7 Website Representative, WP7 Assistant Coordinator, River Cam International, China)

Mr. Stephen Leung (Pfizer Corporation Hong Kong, China)

Mr. Marshall Ma (Link China Pharma Solutions, UK)

Prof. Olavi Pelkonen (Department of Pharmacology, University of Oulu, Finland)

Dr. Daryl Rees (Salupont Consulting, UK)

Prof. Alexander Shikov (St. Petersburg State Medical Academy, Russia)

Dr. Christiane Staiger (Merck Selbstmedikation GmbH, Germany)

Ms. Nadine Su (Link China Pharma Solutions, UK)

Prof. Ian Sutherland (Brunel University, UK)

Ms. Lina Svedlund (presently at Sanofi-Aventis, China; ex-Tasly, China)

Prof. Liping Zhao (Shanghai Jiaotong University, China)

Dr. Shongming Zhong (Honorary Assistant Coordinator, retired from Phynova, UK)

Prof. Zuguang Ye (China Academy of Chinese Medical Science, China)

Advisory Board members

Prof. Gerhard Franz (University of Regensburg, Germany)

Prof. Yi-Tao Wang (University of Macau, China)

Prof. Vivian Wong (Hospital Authority, Hong Kong, China)

Academician Prof. Xinsheng Yao (Jinan University, China)

Year 3 WP7 activities

WP7 members organised and/or lectured in the following meetings:

- The 8th World Congress of Chinese Medicine (London, Sept 2011)
- The 2011 International Symposium on Agricultural Biotechnology: Herbal Medicines for Immunity and Cancer (Taipei, 19-20 Oct 2011)
- The 15th Beijing International Healthcare Industry Forum (Beijing, 1-3 Nov 2011)
- The 5th International Conference on TCM and Diabetes (Chengdu, 4-6 Nov 2011)

- Botanicals/Natural Products Stream at Genesis 2011 in London (1 Dec 2011)

Other GP-TCM activities

- Kelvin Chan convened Joint Workshop in Strasbourg for WP1, WP3 & WP7 in association with some members of EDQM TCM Working Party (see summary below; EDQM = European Directorate for the Quality of Medicines)

Joint Workshop for WP1, WP3 & WP7, Strasbourg

On 29th September 2011, a Joint Workshop for WP1, WP3 & WP7 with some experts from the EDQM TCM Working Party responsible for drafting TCM monographs for the European Pharmacopoeia, was held in Strasbourg.

The Joint Workshop was organised by Prof. Kelvin Chan (Beneficiary member of WP1, WP3, and WP7 and Co-Chair of the SOP Panel for Literature of the GP-TCM) with the help of Prof. Rudi Bauer and Prof. Gerhard Franz (both are non-Beneficiary Advisors of the GP-TCM). The theme of the Workshop was "Quality control of Chinese materia medica (CMM) from a regulatory & toxicological perspective", a topic followed up from the discussion at the 2nd GP-TCM AGM meeting in Braga, July 2011. The participants included: Prof. Rudi Bauer, Prof Kelvin Chan, Prof Pierre Duez, Dr. Tai-Ping Fan, Prof. Gerhard Franz, Mr. Alan Koo, Mr. Erich Stoeger, Prof. Mei Wang, Prof. Liz Williamson, Dr. Kim Wuthold, and Dr. Qihe Xu.

Key discussion points focused on:

1) Regulatory/monographic control on quality issues of CMM decoction pieces and granules and TCM herbal products in EU and China;
2) Research issues on toxico-genomics/omics-related safety issues/approaches in CMM/granules.
3) GP-TCM or its continuum may commence dialogue with granule manufacturers to see if an industry standard can be set to comply with the pharmacopoeia monographs on granules in the future. QC techniques for crude CMM/decoction pieces may not be suitable for granules;
4) Comparison and toxicological evaluation between compositions of granules and CMM;
5) Engaging various members in drafting /reviewing for the JEP Special Issues in particular for WP7 (the regulatory section involving worldwide contributions) and WP3 (studies to demonstrate the reduced toxicity of aconite after processing, boiling in water and mixing with other herbs using Sinitang (consisting of Aconiti Lateralis Radix Praeparata, Zingiberis Rhizoma and Glycyrrhizae Radix et Rhizoma Praeparata Cum Melle), a classical TCM formula as an example.

- Kelvin Chan (and 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*
- Alan Koo attended a lecture by Vice Minister of Health & Commissioner of State Administration of TCM of China "The Role of Chinese Medicine in Further Healthcare Reform in China"

- Tai-Ping Fan edited GP-TCM Newsletters and contributed to Marie-Curie Initial Training Networks application: "Translational Integrative Research on Plant Derived Medicines"(TRAINPLANT)"
- As a Deputy Coordinator of WP9, Tai-Ping Fan co-organised GP-TCM Final Conference and raised funds for GP-TCM Congress

Publications

- Tai-Ping Fan led WP7 team to complete a review on "Future development of global regulations of Chinese herbal products" in *Journal of Ethnopharmacology*
- Olavi Pelkonen led Markku Pasanen, John Linton and some existing WP7 members to complete a perspective "*Omics and its potential impact on R&D and regulation of complex herbal products*" in *Journal of Ethnopharmacology*

Publication of "Future development of global regulations of Chinese herbal products" in *Journal of Ethnopharmacology*

A global overview of regulations on herbal registration has been compiled during the three years of the consortium. The regulatory requirements for registration of herbal products in the EU and China were compared, and this is extended to other regions/countries: Africa, Australia, Brazil, Canada, Japan, Russia, South Korea, Taiwan, and the United States. A wide variation of the regulations for the categories of herbal products exists: food (functional food, novel foods, dietary food for special medical purpose, foods for particular nutritional use, food supplement); cosmetic, traditional herbal medicine products; herbal medicines for human use and veterinary use.

The regulatory issues for registration of herbal products are complicated among the countries and regions worldwide. The information summarised in the text is for reference only. Some regulations which are presented in this review are still in legislation process and may change in due course. Before taking any regulatory action, readers are advised to consult current official legislation and guidance and/or to seek appropriate professional advice. The lessons learnt from global regulation of TCM will provide valuable insights for regulation of other traditional medicine such as Ayurveda and Unani medicine, as well as other forms of indigenous medicine. The WHO is well placed to co-ordinate a consultation process with the aim of putting forward suggestions for harmonisation to key regulatory agencies.

Publication of "Omics and its potential impact on R&D and regulation of complex herbal products" in *Journal of Ethnopharmacology*

In traditional Chinese medicine (TCM), multicomponent and principally plant-derived drugs are used for disease prevention, symptom amelioration and treatment in a personalized manner. Because of their complex composition and consequent multiple targets and treatment objectives, the application of omics techniques and other integrative approaches seems inherently appropriate and even necessary for the demonstration of their potential preclinical and clinical safety and efficacy. This perspectives article provides proposals for the application of omics methods to the investigation of complex herbal products (CHP), including Chinese herbal medicines (CHM), both *in vitro* and *in vivo*, for preclinical and clinical toxicity, pharmacokinetics, pharmacodynamics and efficacy tests. Ultimately, such approaches could aid regulatory scrutiny and potential acceptance, although currently there is no regulatory requirement of omics-based data in any submitted dossier to any regulatory agency, including for conventional drugs and CHP. However, it has been acknowledged that such studies are being increasingly performed, and almost surely will eventually be included into regulatory submission dossiers, possibly initially as supplementary

materials. Specifically for CHM and CHP, omics can play a role both in determining product composition and its variability and in monitoring biological effects in carefully selected platforms. Predicting the future is difficult, but it seems possible that regulatory acceptance of omics techniques and a systems biology approach for the study of TCM, CHM and CHP will not be long delayed. It is expected that current studies and plans employing omics techniques and other integrative approaches will prove to be positive and informative.

Year 3 deliverables

- D7.7 (Programme on R&D of CHM for the Final Conference and submission for publication) – completed.
- D7.8 (Web-based for a on R&D of CHM) – Joint 24/30/36 Report completed. Please refer to the Joint Month 24/30/36 Report.
- In addition, D7.3, D7.4, D7.5 and D7.6 have been updated to reflect our latest activities and achievements. Please refer to individual updated reports.

Year 3 experiences gained and lessons

- Experiences gained and lessons learnt from the two previous years:
    - While others were over-stretched with WP7 activities in addition of other GP-TCM-wide workload, while other members remained inactive, not responding to emails and absent from teleconferences. Thankfully, new members were able to contribute to those countries not covered before, e.g. Korea, Russia.
    - Closer proactive interactions with other WPs very valuable and most essential e.g. Joint Workshop for WP1, WP3 and WP7 with members of EDQM TCM Working Party in Strasbourg on 29th September 2011
    - The WP7 Regulatory article for publication in the *Journal of Ethnopharmacology* was complex because of the number of authors involved. It was most welcome when Alan Koo pulled together all the information from the different authors into the one document for subsequent review by WP7 members. It was clear that to have a single co-ordinator (i.e. Alan Koo) ensured that the article was of a good quality and helped the group to submit within a reasonable timescale
    - With recruitment of 'omics' experts, WP7 now has an excellent network of professionals and experts with good connections who can continue to help raise awareness of Chinese Herbal Medicines at a global level. They can keep the new Association informed of any changes and updates to regulations and technological advances re the use of 'omics' which may be applicable to herbal products.
    - WP7 homepage has been updated and maintained by Alan Koo

- **WP7 summary to Year 1-3**
    - In the past 36 months, WP7 has examined the regulatory requirements for registration of herbal products in the EU and China, as well as other regions/countries: Africa, Australia, Brazil, Canada, Japan, Russia, South Korea, Taiwan, and the United States. We also proposed that regulatory acceptance of omics techniques and a systems biology approach for the study of TCM and

CHP will soon be mandatory. It is expected that current studies and plans employing omics techniques and other integrative approaches will lay a solid foundation for the R&D and future regulation of Chinese herbal medicines.

- These comprehensive studies cumulated in the publication of a review "Future development of global regulations of Chinese herbal products" and a perspective "Omics and its potential impact on R&D and regulation of complex herbal products" in *Journal of Ethnopharmacology*.
- The WHO is well placed to co-ordinate a consultation process with the aim of putting forward *suggestions* for harmonisation to key regulatory agencies.

- **WP plans for future activities towards the extended lifespan of the FP7 GP-TCM project**
  - Tai-Ping Fan invited by *Science* Magazine to co-edit a ~50-page special sponsored feature on TCM in December 2012. It will be written and reviewed by key members of GP-TCM plus top scientists, clinicians, drug developers and regulators across the globe
  - Tai-Ping Fan will continue discussions with members of the UK House of Lords about TCM legislation
  - Tai-Ping Fan in liaison with the FP-7-funded InCrops Project (http://www.incropsproject.co.uk/)
  - Greer Deal and Tai-Ping Fan in preliminary discussions with FP-7-funded PlantLIBRA (PLANT food supplements: Levels of Intake, Benefit and Risk Assessment) about future collaboration

- **WP7 suggestions to the GP-TCM Research Association regarding the future of the area covered by your WP**
  - **Don't forget regulations**!!!!! + importance of translating research to development to commercialization.
  - WP7 can contribute to GP-TCM Research Association by maintaining awareness of changing/updating regulations (globally) applicable to herbal products.
  - WP7 can also make sure that the Association is aware of any consultations being conducted by key bodies/authorities so that the Association can have their say e.g. The UK Government's Red Tape Challenge – Traditional Herbal Medicines (http://www.redtapechallenge.cabinetoffice.gov.uk/medicines-traditional-herbal-medicine/)
  - Connecting people to collaborate for the benefit of all
  - Updates re the use of 'omics' for the development of herbal products
  - Raise global awareness of the Association via knowledge on regulation

- **WP7 Finances**

WP7 was awarded €23,540 for the kick-off and follow-up meetings. The majority of the meeting budget has been used to cover the costs of travelling, accommodation, social events, telecommunication, office stationery and other subsistence. The remaining fund has been used for other WP7-related meetings and the last ~15% has been/are fully committed to cover interactions with WP1, WP2, WP3, WP4, WP5 and WP6, as well as experts in China to answer WP7 central questions, e.g. telecommunication costs and FedEx postage; travel cost to China for the 10th CGCM Meeting in Shanghai and meetings in Beijing with Director QIAN Zhongzhi of Chinese Pharmacopoeia Commission, Division of TCM; travel costs to

Strasbourg; additional travel costs for WP7 members attending GP-TCM Final Conferences and GP-TCM Congress.

- **Final Conclusions of WP7**

As a result of this 3-year study on the impact of omics on global regulations of TCM and herbal medicines, it seems possible that regulatory acceptance of omics techniques and a systems biology approach for the study of TCM and CHP will soon be mandatory. It is expected that current studies and plans employing omics techniques and other integrative approaches will lay a solid foundation for the R&D and future regulation of Chinese herbal medicines.

Discussion session (Led by: Prof. Kelvin Chan)**:**

Please discuss with the modulator of your WP discussion session to specify number of key issues to be discussed, in addition to a Question & Answer session.

- Questions from the floor to be answered by WP7 members.
- Update on Joint Workshop with EDQM-TCM Working Group.
- What individual WP7 members are going to do in the future:
    - To further disseminate GP-TCM activities and achieve their global impact, Tai-Ping Fan to liaise with key members to assemble a team to write articles for the Science Special Issue on TCM in December 2012.
    - Greer Deal and Tai-Ping Fan to interact with PlantLIBRA and identify collaboration opportunities for members of GP-TCM Association.
    - Tai-Ping Fan to introduce the FP-7-funded InCrops Project to GP-TCM Research Association.
    - GRS are organising a workshop on 15th May 2012 in London entitled Asian Traditional Medicines and the EU Herbal Directive.
    - GRS presenting on EU Herbal Directive at Vitafoods European Conference, Geneva, Switzerland on 24th May 2012.
    - GRS organising and promoting Alternative Therapies Stream at Genesis 2012 in London on 13th December.
    - To emphasise how WP7 members will continue to raise awareness of the Association and herbal medicines.

3 MINUTES OF WP7 SESSION AT THE GP-TCM FINAL MEETING IN KERKRADE, THE NETHERLANDS

GP-TCM Final Conference
Rolduc, Kerkrade, the Netherlands
13th April 2012

WP7 Session on Functional Genomics in R&D of Chinese Herbal Medicine

Presenters:
Prof. Kelvin Chan, Universities of Sydney & Western Sydney, Australia
Dr. Tai-Ping Fan, University of Cambridge, UK
Mrs. Greer Deal, Global Regulatory Services (GRS), UK
Mr. Alan Koo, River Cam International, Hong Kong
eProf. Olavi Pelkonen, University of Oulu, Finland

Opening Remarks

Kelvin Chan opened the WP7 Session by commenting that WP7 has the most members and has gone through a lot of changes (not dissimilar to WP5). He explained that both he and Tai-Ping Fan had not been part of WP7 at the outset but had inherited it part way through.

He explained that Tai-Ping Fan would be presenting on the deliverables and issues taken on board by WP7; Greer Deal to present on the regulations applicable to herbal products; Olavi Pelkonen to discuss 'omics' technology and then the session would close with a discussion/Question and Answer opportunity.

Presentations

1) Tai-Ping Fan (TPF), University of Cambridge, UK

TPF admitted that WP7 was not that knowledgeable about functional genomics but that by pooling resources and seeking advice, together members had gathered information and data together. He stated that there were some key players in WP7, namely: Greer Deal, Alan Koo and Olavi Pelkonen and that collectively, this presentation was a celebration of what WP7 had achieved over the past 2.5 to 3 years.

At the outset it was clear that WP7 needed to look at the universal regulatory framework and ultimately it was agreed that they should support the development of harmonised guidelines for the regulation of botanicals by:

- Establishing a collaborative network towards formulating an easy-to-follow statement on the various regulatory frameworks for botanicals, emphasising the synergies and highlighting the differences, in order to contribute to the long-term goal of global harmonisation (*Objective 1*), and
- Reviewing the use of "Omics" in the regulation of drugs and its implication on the R&D of complex herbal medicine (*Objective 2*).

TPF clarified that, with a couple of exceptions, WP7 members were not regulatory experts but having learnt a lot along the way, the objectives were refined (see above bullet points)

Professor Olavi Pelkonen (OP) brought fresh life to the project with his interpretation of "Omics" and how this can be applied to Western medicine as well as Chinese medicine. It

was essential that we had his input so as to include the GP-TCM objective of using a functional genomics approach to WP7's activities.

Next TPF presented slides on WP7s Deliverables: related Central Questions. He confirmed that these appear on the website but are not currently listed in the handbook. All deliverables have been achieved and in some cases exceeded. For example, it was decided to widen WP7's remit further than Europe and China to include input from other key countries and continents: Africa, Australia, Brazil, Canada, Japan, Russia, South Korea, Taiwan and the United States.

By month 24, WP7 was fortunate to enlist OP's contribution re 'omics' technology and complex herbal mixtures.

There has been steady growth of WP7's membership from academia, regulatory agencies (in a personal capacity) and industry. In addition, there have been some very active non-beneficiary members, for example, Greer Deal who is also Deputy Co-ordinator of WP7. And finally, WP7 is well supported by active Advisory Board Members.

Main WP7 activities were summarised as follows:

1. Discuss the problems and solutions in developing Chinese materia medica as proprietary Chinese herbal medicines that meet the market-entry standard NB as from 30th April 2011 unregistered herbal medicines can no longer be sold in Europe. This has had a significant impact on the availability of Chinese Herbal Medicines as well as the Herbal Industry as a whole.
2. Emphasise application of emerging functional genomics technology in this specific area
3. Interface with EMA & SFDA
4. Undertake analysis of the herbal product guidelines in the US FDA and equivalent guidelines in Australia TGA as well as Canada NHPD
5. Consider and undertake analysis of the Guidelines applicable to herbal products in other countries: Africa, Brazil, Japan, Russia, South Korea and Taiwan.
6. Propose a method for reaching a global harmonised registration strategy
7. Search literature beyond herbal products and summarise what has been reported on the application of "omics" in regulation of any drugs and then discuss its implications on regulation of complex herbal products (CHP) and Chinese herbal medicine (CHM)

TPF confirmed that in Year 3, WP7 activities have also included organising, lecturing at or arranging the following meetings/events:

- The 8th World Congress of Chinese Medicine (London, Sept 2011)
- The 2011 International Symposium on Agricultural Biotechnology: Herbal Medicines for Immunity and Cancer (Taipei, 19-20 Oct 2011)
- The 15th Beijing International Healthcare Industry Forum (Beijing, 1-3 Nov 2011)
- The 5th International Conference on TCM in Diabetes (Chengdu, 4-6 Nov 2011)
- Botanicals/Natural Products Stream at Genesis 2011 in London (1 Dec 2011). GD of Global Regulatory Services (GRS) arranges this event in December every year, so if anyone would like to present please contact GD direct.

2) Greer Deal (GD), Global Regulatory Services (GRS), UK

GD provided delegates with a 'snap shot' of the regulations application to herbal products in Europe and avoided going into any detail as this would be a large subject to discuss.

She started with the statement:

"If you don't know what your destination is, how can you plan your journey?".

She stated that it is important to understand what your objectives are but as can be seen by the next slide the destinations themselves are many and can be quite a challenge. As already highlighted by TPF earlier, the EU Directive affecting traditional herbal medicines came into full force last year and has had a significant impact on the industry.

GD was keen to point out that just because a product contains a herbal active in it, you mustn't assume that it has to done the traditional herbal remedy regulatory pathway. There are other routes to market i.e. "think outside the box". GD provided a visual to explain the notion of "thinking outside the box". She suggested that a herbal product could be developed as a:

- Medical Device
- Food Supplement
- Cosmetic
- Vet Product

She emphasised the fact that everyone talks about developing products for human use but that animal use should not be overlooked, it is a viable market.

GD then went on to outline the details of a recent Case Study, details of which are published under Section 2.1.5 of the WP7 regulatory article published in the special issue of the Journal for Ethnopharmacology. She highlighted the fact that the importation of unlicensed medical products into the UK is a criminal offence, the punishment for which can be a fine of circa £50,000 and possibility imprisonment of the company directors. This demonstrated the seriousness of non compliance and that Traditional Chinese Medicines are very much on the radar of the UK's Medicines and Healthcare products Regulatory Agency (MHRA). GD again referred the audience to the published article.

GD highlighted key 'take home' messages:

There are people keeping an eye on the industry, and non-compliance does have significant ramifications

She pointed out that this case study was an example of the ramifications of non compliance but that many UK companies are actually flouting the law. She confirmed that there is currently an on-going battle between those flouting the law and those fully compliant with the latter complaining bitterly that the MHRA are not enforcing the EU Directive in the manner that they should.

GD also mentioned that the UK Government is asking for input from UK companies and individuals about the EU Herbal Directive: should it stay? should it be removed? are there ways in which it can be improved? This input is via the Red Tape Challenge for a 5 week window only. GD reiterated that the Herbal Directive is driven by Europe and therefore, there is only so much that the UK can do.

Next GD discussed initial discussions she and TPF have had with another FP7 funded consortium, PlantLIBRA. It's focus is food supplements re herbs and natural products. Initial discussions have confirmed that there is a synergy between GP-TCM and PlantLIBRA and it would be good to share knowledge and experience with other people at an international level.

GD confirmed that PlantLIBRA's objective is fostering safe use of food products, with emphasis on science base evidence for decision making. She commented that this also underpins GP-TCM. Another PlantLIBRA objective focuses on quality which is also key to GP-TCM: quality of starting material, quality of processes, quality of the regulations themselves, quality of commercialising the products, quality in everything that we do. All of which, again confirms the synergy between the two respective programmes.

3) Tai-Ping Fan (TPF), University of Cambridge, UK

TPF followed with a presentation demonstrating how WP7 interacts with other Work Packages. One key activity was the workshop held in Strasbourg in September 2011 bringing together members from WP1, WP3 and WP7 to discuss "Quality control of Chinese materia medica from a regulatory and toxicological perspective". WP representatives met with EDQM and the discussion focused on:

- Regulatory/monographic control on quality issues of CMM decoction pieces and granules and TCM herbal products in EU and China;
- Research issues on toxico-genomics/omics-related safety issues/approaches in CMM/granules;
- GP-TCM or its continuum may commence dialogue with granule manufacturers to see if an industry standard can be set to comply with the pharmacopoeia monographs on granules in the future. QC techniques for crude CMM/decoction pieces may not be suitable for granules;
- Comparison and toxicological evaluation between compositions of granules and CMM;
- Engaging various members in drafting /reviewing for the JEP Special Issues in particular for WP7.

Next TPF discussed the JEP Review confirming that through the input of key opinion leaders, WP7 was able to formulate an excellent review paper "Future development of global regulations of Chinese herbal products" published in the Journal of Ethnopharmacology:

- Europe
  - Greer Deal liaised with Prof. Werner Knöss
  - (EMA and Federal Institute for Drugs and Medical Devices, Germany)
- China
  - Alan Koo attended a lecture by Vice Minister of Health & Commissioner of State Administration of TCM of China “The Role of Chinese Medicine in Further Healthcare Reform in China”
  - Visited Prof. Guo De-an and Prof. Qian Zhongzhi during and after the CGCM 2011 to collect latest update on the Chinese herbal regulations and their development

- Japan
  - Alan Koo interviewed Prof. Zhao Zhongzhen at the Hong Kong Baptist University and collected latest information on Japanese herbal regulations

TPF then went on to inform the delegates that the first ever authorisation of a traditional herbal medicine outside the European Union had been announced by the Dutch Medicines Evaluation Board (MEB) on 14th March 2012 (to be featured at the conference in Leiden). Admittedly it is made only from a single Chinese herb but at least it is a start.

4) eProf Olavi Pelkonen (OP), Dept of Pharmacology & Toxicology, University of Oulu, Finland (co-opted tox expert of HMPC)

OP presented on the subject of how 'Omics' can be applied in the future.

OP explained that the joined WP about half way through the programme so many of the concepts and notions had already been established. He has aimed to look at "Omics" techniques and systems biology in the context of R&D and also in the regulation of complex herbal products. He explained that much of the material he is presenting has been taken from the article published in the special issue of the Journal of Ethnopharmacology. He pointed out that he wouldn't really call this article a review paper, it is more of a perspectives article as it may well be far too optimistic for the future regulation of Chinese Traditional Medicines and other complex herbal medicines.

OP explained that to change regulations is an extremely slow process often taking many years especially when proposing any major changes to the regulation of pharmaceuticals.

OP then showed a slide which provided the definition of "Omics" according to the US FDA. But that they had omitted to add 'small molecules' so the authors of the published article agreed that this should be added to the original definition!

Next OP provided a very clear flow diagram of the "Omics" Cascade which demonstrated the techniques in order to get a comprehensive view of what happens in the cells of organisms from Genome to Phenotype.

Then he went on to explain "Omics" and regulatory considerations. Formally there are no requirements concerning "Omics" techniques. It is possible to submit this type of data as supplementary information but it is not key for the product assessment. One key reason for this is that "Omics" techniques have not been validated by the regulators. He did confirm, however, that all the major regulatory agencies are in the process of looking at "Omics" studies for future product registrations. In addition, at the EMA, pharmacogenetics/genomics data is submitted on a voluntary basis only but if significant findings have been made the EMA may require pharmacogenics control studies.

In OP's opinion there are distinct possibilities for using "Omics" techniques for the development of products with a TCM background because TCMs are complex plant based medicines which are difficult to study with conventional approaches. OP concluded by demonstrating how "Omics" can be used in both preclinical and clinical phases.

5) Tai-Ping Fan (TPF), University of Cambridge, UK

TPF brought the main part of the WP7 session to a close by confirming how the WP7 budget was spent and itemising the conclusions which were reached by WP7 as follows:

- The regulatory issues for registration of herbal products are complicated among the countries and regions worldwide.
- The lessons learnt from global regulation of TCM will provide valuable insights for regulation of other traditional medicine such as Ayurveda and Unani medicine, as well as other forms of indigenous medicine.
- The WHO is well placed to co-ordinate a consultation process with the aim of putting forward suggestions for harmonisation to key regulatory agencies.
- It seems possible that regulatory acceptance of omics techniques and a systems biology approach for the study of TCM and CHP would soon be mandatory.
- It is expected that current studies and plans employing omics techniques and other integrative approaches will lay a solid foundation for the R&D and future regulation of Chinese herbal medicines.

TPF also made delegates aware that even though WP7 had an extensive membership, many members are opinion leaders with significant demands on their time and therefore, it was difficult to absorb WP7 activities on top of existing demands. Recent new members, however, from South Korea and Russia helped to produce a more rounded regulatory article for JEP along with Alan Koo acting as the central co-ordinator ensuring that WP7 pooled their resources resulting in a good quality review article.

TPF also highlighted the fact that WP7 now has a well-established global network of professionals which was not anticipated even only year ago. TPF also confirmed that not all WP7 members are from academia and he thanked industry members in particular for their input because to ensure GP-TCM deliverables are accomplished they have to take time away from work (invariably this is unpaid time).

Finally, TPF announced that as a legacy for GP-TCM, he has been invited by AAAS Science magazine to edit a special sponsored issue on TCM in December 2012. In addition, a very unexpected outcome is that TPF has been involved in discussions at the UK's House of Lords regarding the future registration of TCM which demonstrates their interest in the regulation of Chinese medicines.

6) Professor Kelvin Chan (KC), Universities of Sydney & Western Sydney, Australia

KC then led the WP7 Final Report Discussion. He showed a few slides on the EDQM meeting to highlight the interaction between WPs 1, 3 and 7 as well as 6 and was pleased to feedback that quality, safety and efficacy all comes together in one place. In the future, it would be good for regulatory people to understand why TCM can be linked with systems biology to explain the mechanisms of action and why it is we talk about "personalised medicine". The Chinese had "personalised medicine" 5,000 years ago i.e. TCM is based on personal assessment and treatment.

KC also reiterated that there is a legacy to the GP-TCM consortium in the form of the GP-TCM Research Association. He confirmed that one hour in the evening has been assigned to discuss the new Association and that all members attending the Rodulc conference can be Association members for one year free-of-charge.

KC then asked the Floor for feedback and questions:

Brian Clark, CSO, PhytAge ApS:
Expressed his astonishment that WP7 had "ignored India" and that 1.4 billion Indians should not be ignored.

TPF responded that WP7 had only a certain amount of time and resources to pull all of the information together and that it was not possible to cover all areas of the world. He also mentioned that the next phase with EDQM will include Ayurvedic medicine.

Brian also commented that activities were very EU-centric and assumes this is because GP-TCM is reliant on EU funding. He advised that the future Association should research into resources from outside Europe. This is of particular relevance when you consider the current direction of Europe and the cuts to science within the EU. His fear is that the EU will become 'second rate' and therefore, it is important to engage with a region which will invest in science i.e. Asia.

TPF invited *Professor Geoffrey Burnstock (President, Autonomic Neuroscience Centre; Convener, Centre for Neuroscience)* to comment:
He replied that he was not really aware of Ayurvedic medicinal practitioners in the UK and that to include Ayurvedic medicine in the future would be an "exciting marriage".

Rob Verpoorte: Rob offered some further clarity by stating that "this is a model for traditional medicine all over the world - we are setting the standards for the future i.e. rules to study traditional medicine. We need to start somewhere it is a major effort from everyone to set the standards."

KC responded that he felt it was important to make it clear that Chinese medicine is being used as an example and that lessons learnt from this can be 'spun out' to incorporate other native medicines and systems. He also explained that much of the documentation for TCM is available only in Chinese which is yet another difficulty to overcome. So again lessons can be learnt from this for translating other non-English documents. KC also informed the meeting that his team had received £20,000 funding from the Australian Government and he felt that this was an important step in getting the Australian Government to take notice of Chinese Medicine. He responded to Brian that he appreciated his comment regarding India but that the consortium needed to focus on one example and in this instance, it was Chinese Medicine.

Qihe Xu also contributed by stating that they had made a big effort to include Societies from elsewhere such as France. Brian also advised that Greece should also be a focus because they have a very long history with regards to medicinal herbs.

Professor Burnstock advised delegates that, in his experience, successful organisations (whether departments, research institutes etc) have quality people. What makes something successful is the people, not the money or the organisations but the people. It is people who make things happen.

Qihe Xu's final comment was that the GP-TCM, both now and its legacy, is inclusive and not exclusive and will never exclude interested members.

KC ended the meeting by asking members to "help us make it better".