

The 8th Global Summit on Regulatory Science Conference (GSRS2018)

Risk/Benefit of Dietary Supplements and Herbal Medicine in the Era of Data Science

National Institutes for Food and Drug Control (NIFDC)

NIFDC Conference Hall, Beijing, China

September 26-27, 2018



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PROGRAM AT A GLANCE

GSR2018

September 26-27, 2018

NIFDC Conference Hall, Beijing, China

Wednesday, Sept. 26, 2018	Wednesday, Sept. 26, 2018	Thursday, Sept. 27, 2018	Thursday, Sept. 27, 2018
DAY 1	DAY 1	DAY 2	DAY 2
Session 1 (Morning)	Session 2 (Afternoon)	Session 3 (Morning)	Poster Session
Regulatory Needs – Global Perspective in the 21st Century	Challenges and Opportunities	Safety and Quality Assessment	Session 4 (Afternoon)
8:00 - 12:00	1:00 - 5:30	9:00 - 12:00	Data Analytics and Emerging Methodologies
			1:00-5:00

General Information

Venue and Date:

- National Institutes for Food and Drug Control (NIFDC) Campus, NIFDC Conference Hall, Beijing, China
- September 26-27, 2018 (Wednesday and Thursday)

Scientific Program Committee:

- Co-Chairs: Weida Tong (National Center for Toxicological Research (NCTR)/Food and Drug Administration (FDA), USA and Elke Anklam (European Commission, European Union)
- Global Coalition for Regulatory Science Research (GCRSR) Executive Committee and GCRSR Bioinformatics Working Group

Conference Coordinator:

- Roben Brooks (rbrooks@aralliance.org)

Local Organizing Committee Administrator:

- Dr. Xingchao Geng (gengxch@nifdc.org.cn or gengxch@126.com).

Conference Hotels (Logistical Information):

It is recommended that conference participants stay in one of the two GSRS2018 recommended hotels (see detailed instructions below), particularly those attending from the countries outside of China. These two hotels are close to each other but not in the walking distance. The hotels are about 40 minutes (driving) away from the GSRS2018 meeting venue. Shuttle buses will be provided to those staying in these two hotels. Please inform Dr. Xingchao Geng (gengxch@126.com or gengxch@nifdc.org.cn) about which hotels you are staying at and if you need to ride the shuttle buses to the conference. Dr. Geng must receive this information **no later than four (4) weeks** before the conference.

The shuttle bus will leave your hotel at 7:00AM on 26th (Day 1) and 7:50AM on 27th (Day2)

GSRS2018 Recommended Hotel #1:

Beijing Qianmen Jianguo Hotel (北京前门建国饭店)

Beijing Qianmen Jianguo Hotel website: http://www.qianmenhotels.com/en/hotel_info.html

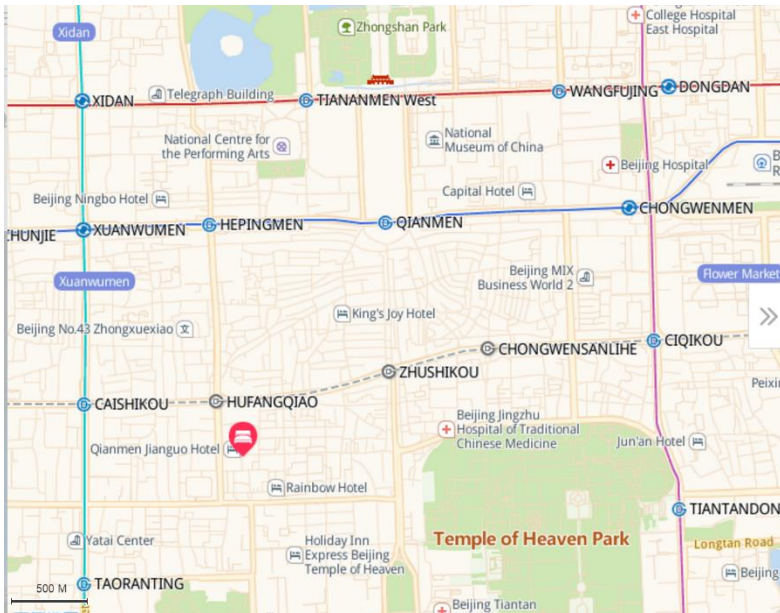
Address 175, Yong An Road Xuan Wu District Beijing China. (北京市宣武区永安路175号)

Telephone: 8610-51291066

Fax: 8610-61010882

E-mail: sales@qianmenhotels.com

Nearest metro station (200m, ~5min walk): Hufangqiao on line 7.



There are three (3) options for booking/reserving this hotel:

1. Reserve a room at the conference rate: We have reserved a block of rooms at the Beijing Qianmen Jianguo Hotel (北京前门建国饭店) at a conference rate. If you wish to reserve a room at this hotel, please contact Dr. Xingchao Geng (gengxch@126.com or gengxch@nifdc.org.cn) and provide the following information:
 - a. Full name as it appears in your passport
 - b. Passport number
 - c. Organization name and address
 - d. If additional person(s) will be lodging with you, please provide his or her full name and passport number.
 - e. Check-in and check-out dates.
 - f. Selection of room type: ¥620 (~\$100, guest room, 单间, including one breakfast), ¥580 (~\$93, standard room, 标间, including one breakfast), ¥690 (~\$110, executive room, 套间, including two breakfasts).
2. Reserve a room directly from the hotel website: If you use the link provided above to reserve a room, it's important to know the price might be ¥200 (~\$32) more than the rate quoted above.
3. Reserve a room using other options: You may use Expedia, Ctrip, hotel.com, or other similar online booking systems to reserve a room; however, the room rates via this method of making reservations have not been investigated.

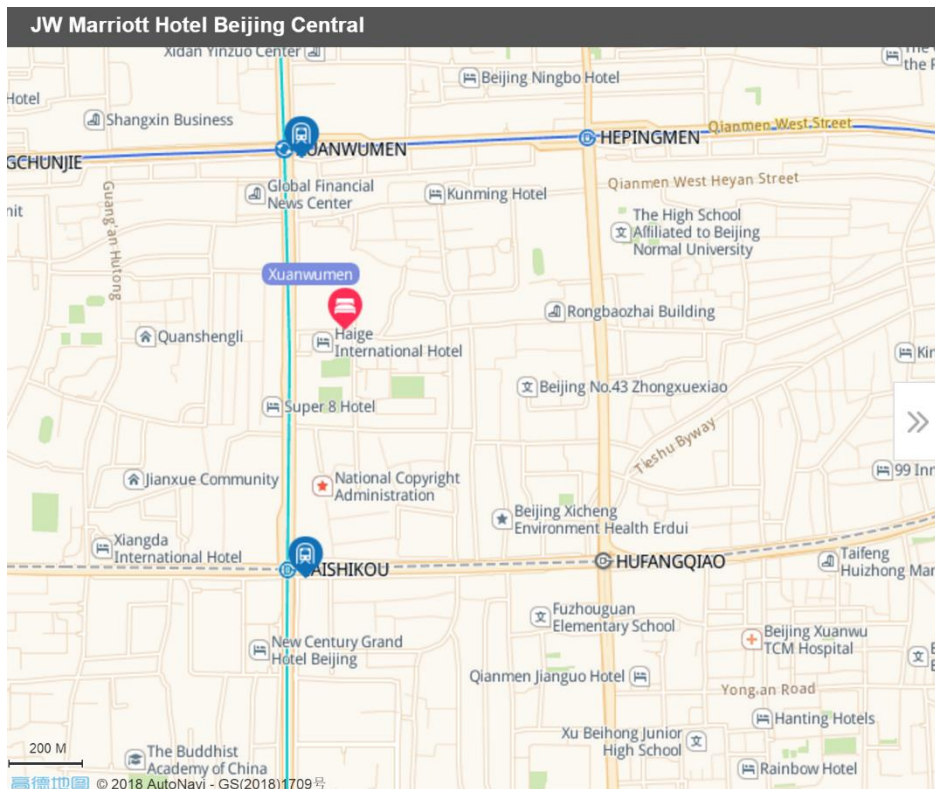
GSR2018 Recommended Hotel #2:

JW Marriott Hotel Beijing Central

Nol.18 Xuanwai Street Xidan and Financial Street Area Beijing 100052 China | 0.57km from Metro Station:Xuanwumen

[JW Marriott Hotel Beijing Central Website: http://jw-marriott-hotel-beijing.31td.com/index.html](http://jw-marriott-hotel-beijing.31td.com/index.html)

<https://www.trip.com/hotels/beijing-hotel-detail-997715/jw-marriott-hotel-beijing-central/>



We have no conference rate for this hotel and please reserve your own room.

Transportation to the GSR2018 recommended hotels from the Beijing Capital International Airport:

- Beijing Capital International Airport (PEK) is the primary airport most participants (particularly those from outside of China) will use.
- The best method of transportation is taxi. The taxi ride from the airport to both hotels is approximately one (1) hour; and the taxi cost is **¥150 (~40km)**. Below are the signs with Chinese characters you may use to communicate with the taxi driver to the hotels.

Easy way to the Qianmen Jianguo Hotel

Below is for the hotel's Chinese address and telephone number (which is a jpeg image). You can print it and show to the local taxi driver, which means Mr. Driver, please take me to Qianmen Jianguo Hotel and our address...

司机先生请带我去前门建国饭店:

北京前门建国饭店

地址: 北京市宣武区永安路175号

Easy way to the JW Marriott Hotel Beijing Central

Nol.18 Xuanwai Street Xidan and Financial Street Area Beijing 100052 China

Below is for the hotel's Chinese address and telephone number. You can print it and show to the local taxi driver, which means Mr. Driver, please take me to JW Marriott Hotel Beijing Central and our address...

司机先生请带我去

北京粤财JW万豪酒店

地址: 北京市西城区宣武门外大街18号

电话: 9501 3760 8818

- Please provide your flight information (date/time, airline, and flight number) to Dr. Xingchao Geng (gengxch@nifdc.org.cn or gengxch@126.com). Once received, Dr. Geng will evaluate whether it is possible for you to be picked by NIFDC as a courtesy. Availability for this service is dependent upon the number of GSRS2018 participants arriving within a reasonable timeframe.
- If you arrive from a different airport other than the Beijing Capital International Airport (PEK) and need directions to your hotel, please contact Dr. Xingchao Geng (gengxch@nifdc.org.cn or gengxch@126.com).

GSRS2018
PROGRAM AGENDA

DAY 1 - SEPTEMBER 26, 2018

8:00-9:00 am Registration and Poster Setup

8:30-8:50 am *Opening Remarks*

- Deputy Director, China Food and Drug Administration (CFDA), CHINA (TBD but committed)
- William (Bill) Slikker, Jr., Co-Chair, Global Coalition for Regulatory Science Research (GCRSR), USA

SESSION 1: REGULATORY NEEDS – GLOBAL PERSPECTIVE IN THE 21ST CENTURY

Co-Chairs: Li Bo, Director of NIFDC, CHINA and William Slikker, Director of NCTR/FDA, USA

8:50-9:05 am *Dietary Supplement vs Drug*, Latasha A. Robinson, U.S. Food and Drug Administration (FDA), USA

9:05-9:30 am *Development of Regulatory Science in China*, Changxiao Liu, Academician, Tianjin Institute of Pharmaceutical Research, Tianjin Binhai Center for Food and Drug Regulatory Science, CHINA

9:30-9:55 am *The Rules on Dietary Supplements in the European Union (EU)*, Gudrun Gallhoff, Directorate-General, Health and Food Safety (DG SANTE), EU

9:55-10:20 am *Safety and Benefit Assessment of Food Supplements in the European Union*, Valeriu Curtui, Head of the Nutrition Unit, EFSA, ITALY

10:20-10:45 am *Break*

10:45-11:10 am *Recent Progress in Approval Systems for Herbal Medicines in Japan*, Takashi Hakamatsuka, Head, Division of Pharmacognosy, Phytochemistry and Narcotics, National Institute of Health Sciences (NIHS), JAPAN

11:10-11:35 am *Food Supplements: Methodology Used in the Brazilian Regulation*, Stefani Faro de Novaes, Sanitary Regulation and Surveillance, Brazilian Health Regulatory Agency (ANVISA), BRAZIL

11:35-12:00 pm *An Australian Perspective on Herbal Medicines Regulation—Growth and Opportunity in the Age of Data*, Adam Cook, Complementary and Over the Counter Medicines Branch, Therapeutic Goods Administration (TGA), Australian Government Department of Health, AUSTRALIA

12:00-1:00 pm Lunch (NIFDC Cafeteria)

SESSION 2: CHALLENGES AND OPPORTUNITIES

Co-Chairs: Elke Anklam, European Commission, EU and Junzhi Wang, NIFDC, CHINA

- 1:00-1:25 pm** ***Assessing Public Health Risk for Novel Foods and Novel Food Ingredients***
Scott Crerar, Science and Risk Assessment, Food Standards Australia New Zealand (FSANZ), AUSTRALIA
- 1:25-1:50 pm** ***Improving the Drug Review System to Accelerate New Drug Development in China***, Zengjun (Alex) Xu, Chief Scientist, Center for Drug Evaluation, China National Drug Administration, CHINA
- 1:50-2:15 pm** ***The European Food Safety Authority's Approach on Data for Safety and Benefit Assessment in the Area of Food Supplements***, Marta Hugas, Chief Scientist, European Food Safety Authority (EFSA) and Valeriu Curtui, Head of the Nutrition Unit, EFSA, ITALY
- 2:15-2:40 pm** ***Botanical Drug Product Regulation in FDA***, Jing Li, Center for Drug Evaluation and Research, Food and Drug Administration, Maryland, USA
- 2:40-3:05 pm** ***Break***
- 3:05-3:30 pm** ***Challenges and Strategies for Safety Assessment of Health Food in China***, Bo Li, Department of Food Risk Assessment, Institute for Food Control, NIFDC, CHINA
- 3:30-3:55 pm** ***Regulation and Safety Assessment of Supplemented Foods - A Canadian Perspective***, William Yan, Director of the Bureau of Nutritional Sciences, Health Canada, CANADA
- 3:55-4:20 pm** ***Safety Assessment of Dietary Supplements Containing Medicinal Herbs in Korea***, Jong Kwon Lee, Director, Toxicological Research Division, National Institute of Food and Drug Safety Evaluation (NIFDS), Ministry of Food and Drug Safety (MFDS), KOREA
- 4:20-4:45 pm** ***The future of the "Botanical Drugs" paradigm requires strong international regulatory harmonization***, Cesar Compadre, University of Arkansas for Medical Sciences (UAMS), Arkansas, USA
- 4:45-5:30 pm** ***Panel Discussion***

DAY 2 - SEPTEMBER 27, 2018

SESSION 3: SAFETY AND QUALITY ASSESSMENT

Co-Chairs: Primal Silva, Canadian Food Inspection Agency (CFIA), CANADA and Yan Huo, NIFDC, CHINA

9:00-9:20 am	<i>A Need for Comprehensive Approach to Assess the Quality and Safety of Botanicals/Dietary Supplements</i> , Ikhlas A. Khan, Director, National Center for Natural Products Research, University of Mississippi, USA
9:20-9:40 am	<i>Mutational Signature Analysis for Molecular Cancer Epidemiology: the Example of Aristolochic Acid</i> , Steven G. Rozen, Duke National University Singapore (NUS) Medical School, SINGAPORE
9:40-10:00 am	<i>Dietary Supplements and Food Fraud</i> , Franz Ulberth, Joint Research Centre (JRC), EU, ITALY
10:00-10:30 am	<i>Break</i>
10:30-10:50	<i>Toxicological Evaluation of Dietary Supplements Using the Emerging and Conventional Methodologies</i> , Nan Mei, National Center for Toxicological Research, Food and Drug Administration, USA
10:50-11:10 am	<i>Concerns of Herbal Product-Induced Toxicity</i> , Amy C. Brown, Department of Complementary & Integrative Medicine, John A. Burns School of Medicine, University of Hawaii at Manoa, USA
11:10-11:30 am	<i>New Approaches and Special Consideration for Safety Assessment of Herbal Drugs</i> , Xingchao Geng, NIFDC, CHINA
11:30-12:00 am	<i>Panel Discussion</i>
12:00-1:00 pm	Lunch
1:00-2:00 PM	POSTER SESSION

SESSION 4: DATA ANALYTICS AND EMERGING METHODOLOGIES

Co-Chairs: Weida Tong (NCTR/FDA, USA) and Marta Hugas (EFSA, EU, ITALY)

2:00-2:20 pm	<i>USP Botanical Standards – A Comprehensive Approach for Quality</i> , Nandu Sarma and Nurisha Rush, United States Pharmacopeia (UPS), Rockville, Maryland, USA
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2:20-2:40 pm	<i>Establish Genomic Reference for Chinese Herbal Medicine Towards Health Food Safety</i> , Professor Chang Liu, Institute of Medicinal Plant Development, Chinese Academy of Medical Science, CHINA
2:40-3:00 pm	<i>Developing Safer Botanical Medicine Using Chemoinformatics Approaches</i> , Shraddha Thakkar, National Center For Toxicological Research, Food and Drug Administration, USA
3:00-3:30 pm	<i>Break</i>
3:30-3:50 pm	<i>Advancing Quality Control of Botanical Drugs Using Computational Methods: A Case Study of Panax Notoginseng</i> , Xiaohui Fan, Vice Dean, College of Pharmaceutical Sciences, Zhejiang University, CHINA
3:50-4:10 pm	<i>Emerging Technologies for the Quality Control and Activity Screening of Chinese Herbal Medicine</i> , Qionglin Liang, Director, Modern Research Center of Traditional Chinese Medicine and Co-Chair of Department of Chemistry, Tsinghua University, CHINA
4:10-4:30 pm	<i>Innovative Research on Herbal Inhalation Therapy</i> , Ruchi Singh, Dev Sanskriti Vishwavidyalaya, Gayatrikunj-Shantikunj, Haridwar (Uttarakhand), INDIA
4:30-5:00 pm	<i>Panel Discussion</i>
5:00-5:10 pm	<i>Closing Remarks</i>

Biographies: Session Co-Chairs

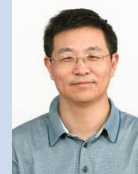
Co-Chairs for Morning Session 1 (September 26th):

Bo Li, Ph.D.

Director

National Institutes for Food and Drug Control (NIFDC)

Beijing, CHINA



Dr. Li Bo is Director General of National Institutes for Food and Drug Control (NIFDC), China National Drug Administration (CNDA), and also Chairman of Council for Bioassay, China Pharmacopoeia Committee, and Chairman of Council for Drug Safety Research and Evaluation, Chinese Pharmaceutical Association. His main research works is on safety evaluation drugs. He firstly established a safety evaluation system in accordance with the international GLP standards in China, presided over 11 national and provincial projects, developed some new technologies and new methods on immune toxicity, biological distribution, tissue cross reactivity, and new biomarkers. Leading the academic field of the safety evaluation of biotech drugs, he established the academic committee in this field to promote the standardization development of GLP in China. He also developed a series of technical standards for the national standard of bacterial endotoxin, which had independent intellectual property rights in China, and improved the quality control level of products and ensured the drug safety. He is the recipient of several public health awards such as the second prize of China National Science Progress Award and the second prize of the Beijing Science Progress Award. Dr Li published widely in journals and books in the field of drug safety and quality. He is the author of *Safety Evaluation of Biotechnology Pharmaceuticals* and *Methodology of New Drug Research in Toxicology et al.*

Dr. Bo serves on behalf of the National Institutes for Food and Drug Control (NIFDC), China National Drug Administration, as an Executive Committee member on the Global Coalition for Regulatory Science Research (GCRSR).

William Slikker Jr., Ph.D.

Director

National Center for Toxicological Research (NCTR)

U.S. Food and Drug Administration (FDA)

Arkansas, USA



Dr. William Slikker, Jr. is the Director of FDA's National Center for Toxicological Research (NCTR). He received his Ph.D. in Pharmacology and Toxicology from the University of California at Davis. Dr. Slikker holds adjunct professorships in the Departments of Pediatrics, and Pharmacology/Toxicology at the University of Arkansas for Medical Sciences. He is currently associate editor for *NeuroToxicology* and for *Experimental Biology and Medicine*. He has served as president of the Academy of Toxicological Sciences, the Teratology Society and the Society of Toxicology. Dr. Slikker has co-authored over 350 publications in the areas of transplacental pharmacokinetics, developmental neurotoxicology, systems biology, and risk assessment.

Co-Chairs for Afternoon Session 2 (September 26th):

Elke Anklam Ph.D.

Director of Directorate F: Health, Consumers, Reference Materials at the Joint Research Center of the European Commission
Ispra/ITALY – Geel/BELGIUM



Dr. Elke Anklam is a chemist, with specialization in food, organic and radiation chemistry. After obtaining her PhD from the University Hamburg, Germany, she worked in various European Research Institutions and was a Teaching Professor at the Applied University of Fulda, Germany. Since 1991, she has been working at the European Commission's Joint Research Center (EC-JRC). From 2006-2012, she was Director of the JRC-Institute for Health and Consumer Protection (IHCP) in Ispra, Italy and from 2012 – July 2016, Director of the JRC-Institute for Reference Materials and Measurements in Geel, Belgium. Since July 2016, she is the Director of the JRC-Geel site and the new JRC Directorate F: Health, Consumers & Reference Material (a merger of the former IHCP and IRMM), located at the JRC-Geel and JRC-Ispra site.

Junzhi Wang

Chief Scientist and Former Deputy Director
National Institutes for Food and Drug Control (NIFDC)
Beijing, CHINA



Junzhi Wang is the chief expert in the field of Biological Products Quality Control in NIFDC, and also the director of WHO Collaborating Center for standardization and evaluation of biologicals in China. In 1993, Professor Wang got his MD degree from Mie University in Japan. After returning to China in 1995, he presided over the establishment of the key technology system of biological drug quality control and safety evaluation in accordance with international standards, including establishment of reference standard material and novel methods. The system has been applied in quality standard researches for over 200 innovated biologicals, ensuring the quality of innovated biological drugs and providing technical support for regulatory decision in China.

He published 91 papers as first or corresponding authors in journals embodied in the Science Citation Index, including *NEJM*, *Lancet*, *Nature*, *Science*, and so on. Also he wrote three monographs, including “Research, development and quality control of biological products” and “Quality control and evaluation of vaccines”, which give guidance for manufacturers and promote the development and industrialization process of biologicals in China. He received the second prize of the national awards four times. Other honors awarded include the Contribution Award of Promoting Development of Public Health and Preventive Medicine, the May Day Labor Medal of the Central Government Departments, the National Advanced Worker Award, and the 2012 Bethune Medal.

Co-Chairs for Morning Session 3 (September 27th):

Primal Silva, BVSc, Ph.D.

Acting Vice-President
Chief Science Operating Officer
Canadian Food Inspection Agency (CFIA)
Ottawa, CANADA



Dr. Primal Silva is the Acting Vice President and Chief Science Operating Officer at the Canadian Food Inspection Agency (CFIA), Canada's largest federal science-based regulatory government agency. He provides strategic direction and national Canadian leadership development and implementation of science strategies as well as science engagement with national and international partners. Dr. Silva is responsible for the national CFIA Laboratory Network which is mandated to uphold food safety, animal health and plant health in order to enhance the well-being of Canada's people, environment and economy. Dr. Silva is a veterinarian who obtained a PhD from the University of Sydney, Australia, in 1987 and conducted post-doctoral studies at McMaster University and at the Ontario Veterinary College, University of Guelph. He joined the Federal Public Service in 1993 where he has held several positions with increasing responsibilities. He is also a contributing member to numerous committees and working groups at both the domestic and international levels including the Scientific Advisory Body of the Organisation for Economic Co-operation and Development (OECD), Global Coalition for Regulatory Science Research (GCRSR), and the International Research Consortium on Animal Health (STAR-IDAZ).

Dr. Yan Huo, Ph.D. /Professor

Director of General Toxicology Department
National Center for Safety Evaluation of Drugs
National Institutes for Food and Drug Control (NIFDC)
Beijing, CHINA

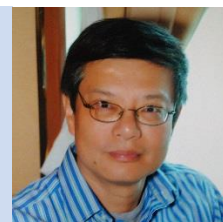


Dr. Yan Huo, received her B.S. and M.S. degrees in Pharmacy from Shenyang Pharmaceutical University. She received her Ph.D degree in Biochemistry and Molecular Biology in The Fourth Military Medical University. She worked as a visiting scientist in NIHS in Japan and in NIEHS in USA in 2001 and 2014 , respectively. Dr. Huo has over 19 years experiences in toxicology research and drug safety evaluation. Her major area is the safety evaluation of biotech-derived pharmaceuticals. She has authored 30 scientific publications in journals (2 SCI journals) and given over 30 presentations at national and international professional meetings. She are the Heads or group leader of 9 research projects funded by National Science and Technology Major Projects for "Major New Drugs Innovation and Development" in 11th, 12th and 13th five-year plans. She won Second Class Awards of National Award for Science and Technology Progress (9th people), from The Ministry of Science and Technology of P.R.China in 2008.

Co-Chairs for Afternoon Session 4 (September 27th):

Weida Tong, Ph.D.

Director, Division of Bioinformatics and Biostatistics
National Center for Toxicological Research (NCTR)
U.S. Food and Drug Administration (FDA)
Arkansas, USA



Dr. Weida Tong is Director of Division of Bioinformatics and Biostatistics at FDA's National Center for Toxicological Research (NCTR/FDA). He has served science advisory board for several multi-institutional projects in Europe and USA. He also holds adjunct appointment at several universities. In addition, he is the founder and board chairperson of newly established international MAQC Society. His division at FDA is to develop bioinformatic methodologies and standards to support FDA research and regulation and to advance regulatory science and personalized medicine. The most visible projects from his group are (1) conducting the Microarray and Sequencing Quality Control (MAQC/SEQC) consortium to develop standard analysis protocols and quality control metrics for emerging technologies to support regulatory science and precision medicine; (2) development of liver toxicity knowledge base (LTKB) for drug safety; (4) *in silico* drug repositioning for the enhanced treatment of rare diseases; and (4) development of various tools such as ArrayTrack™ suite to support FDA review and research on pharmacogenomics. In addition, his group also specializes in molecular modeling and QSARs with specific interest in estrogen, androgen, and endocrine disruptor. Dr. Tong has published more than 250 papers and book chapters.

Marta Hugas, BSc, MSc, Ph.D.

Chief Scientist
European Food Safety Authority (EFSA)
ITALY, EU



Dr Marta Hugas is serving as Chief Scientist at the European Food Safety Authority. This position addresses the development of EFSA's scientific strategic direction; acting as focal point on scientific matters and facilitating the understanding of science; fostering scientific cooperation as well as leveraging connections and networks for promoting EFSA's research priorities. She joined EFSA in 2003 and since then Marta has held several positions: Head of Biological Hazards Unit (BIOHAZ), Head of the Risk Assessment and Scientific Assistance Department a.i. (RASA) and Head of the Biological Hazards and Contaminants Unit (BIOCONTAM).

Marta holds a BSc in biological sciences, an MSc in genetics and microbial biotechnology and a PhD in food microbiology. Prior to joining EFSA, she worked for the Institute for Food and Agricultural Research and Technology (IRTA) in Spain, where she was Head of the Food Microbiology and Biotechnology Unit and led a research group on applied research on meat and food safety. From 1992 to 2004 she was an Associate Professor at the University of Barcelona. Marta's areas of expertise focus on: food hygiene, development of starter and bio protective cultures, probiotics for the safety of poultry meat, emerging preservation technologies as well as risk assessment of biological hazards. Dr Hugas has extensively published papers and book chapters.

Biographies and Abstracts of Speakers (Alphabetically ordered by last name)

Amy C. Brown Ph.D., RDN

Department of Complementary & Integrative Medicine, John A Burns School of Medicine
University of Hawaii at Manoa
Hawaii, USA



Dr. Brown's research and teaching expertise are within the Department of Complementary and Integrative Medicine at the University of Hawaii's John A. School of Medicine. She has authored over 30 scientific and lay publications including the Academy of Nutrition and Dietetic's position paper on Functional Foods. Her research explores the anti-cancer effects of poi, noni, ginger, and guava, the possible probiotic effects of poi (Hawaiian probiotic) in a clinical trial, the potential of kukui (Hawaii's state tree) nut oil as a topical treatment for psoriasis, the possible role of diet in treating Crohn's disease, ulcerative colitis, lupus erythematosus and autism, and testing for liver toxicity in Pacific Islander kava beverage drinkers. Dr. Brown's early publications pursued the use of different plants common in Hawaii that might be used in the complementary treatment of various diseases. She was interested in finding out if certain local plants in Hawaii had extracts with potential anti-cancer activity. She studied the potential anti-cancer (anti-proliferative) effects of several food extracts found in Hawaii - poi, noni, ginger, and guava – and they were all found to have anti-proliferative effects on certain cancer cell lines. She has previously collaborated with Dr. Martin Jadus of the Veterans Hospital in Long Beach, CA. The resulting publications have received quite a bit of international attention and been downloaded more frequently than any of my other articles by both public and private organizations. Dr. Brown's total downloads in ResearchGate of 30+ peer-reviewed journal articles exceed 2,200. These natural plant sources of possible anti-cancer substances set the stage for future research by others in searching for new and effective cancer drugs.

Liver, Kidney, Heart and Cancer Toxicity Cases Related to Herbs and Dietary Supplements: An Online Table of PubMed Case Reports

The National Institutes of Health and National Institute of Diabetes and Digestive and Kidney Diseases have an online website [LiverTox.nih.gov] listing drugs, herbs, and dietary supplements with possible adverse effects, but the list is not online for continual updating.

Aims: To create an online research summary table of liver, kidney, heart, and cancer toxicity case reports related to DS toxicity in PubMed that are related to Dietary Supplements (DS). **Methods:** Documented PubMed case reports (1966 to June, 2016, and cross-referencing) of DS appearing to contribute to liver, kidney, heart, and cancer toxicity were listed in "Toxic Tables." The broad search included the keywords of "plant extracts" or "plant preparations" with "the organ" and "toxicity." Case reports were excluded if they involved herb combinations (some exceptions), Chinese herb mixtures, mixed herb containing teas, mushrooms, poisonous plants, self-harm, excessive doses (except vitamins/minerals), legal or illegal drugs, drug-herbal interactions, and existing confounders (drugs or diseases). **Results:** The number of published case reports related to DS Toxicity in PubMed in the last 50+ years (1966 to May 2016) included: Approximately 21 herbs and 14 DS related to liver injury case reports. Approximately 7 herbs (minus 4 no longer for sale), 10 dietary supplements (minus 3 excluded due to excessive doses and 1 herb no longer sold), and four foods have been related to kidney injury case reports. Four traditional Chinese medicine herbs, 1 Ayurvedic herb, 2 North American herbs, and 1 food were related to heart case studies. One herb, 0 dietary supplements, and 2 foods were related to cancer cases. **Conclusion:** This online "Toxic Table" provides clinicians, consumers, and manufacturers a list of DS that can be constantly updated to serve as a warning to possibly reduce the number of future DS toxicity cases.

Adam Cook, Ph.D.

Complementary and Over the Counter Medicines Branch
Therapeutic Goods Administration (TGA)
Australian Government Department of Health
AUSTRALIA



Dr Adam Cook is Acting Director of the Listing Compliance Section within the Complementary and OTC Medicines Branch of the TGA. Adam received his Bachelor and Doctorate degrees in Medical Sciences from the University of Sydney and conducted postdoctoral research in cell biology and immunology at the Institut Curie (Paris), Australian National University and University of Sydney, before joining the TGA. Previously a regulatory toxicologist involved in the pre-market evaluation of prescription medicines at the TGA, Adam currently oversees the monitoring and enforcement of regulatory compliance for herbal and complementary medicines and other low-risk products that are supplied in Australia.

An Australian Perspective on Herbal Medicines Regulation—Growth and Opportunity in the Age of Data

In Australia, herbal medicines and many dietary supplements are regulated as medicines within the therapeutic goods regulatory framework, providing enviable consumer confidence in the quality and safety of these products. However, commensurate with the low risk posed to consumers, most are regulated as self-selected ‘listed’ medicines that can be marketed without any pre-market approval of the product by the TGA, as long as they meet certain eligibility criteria to ensure quality and safety. Effective post-market monitoring of compliance with regulatory requirements therefore plays a pivotal role in maintaining consumer safety and confidence in listed medicines. Booming consumer interest and consumption of complementary medicines domestically and abroad and thus considerable growth of the number of listed medicines on the market, coupled with the Australian Government’s deregulation agenda, raises key challenges for the TGA’s compliance monitoring program. To respond to these challenges and continued innovation in herbal medicines development, the TGA is pursuing several reforms and innovations, including the use of data analytics. This presentation will explore the unique elements of the framework for herbal medicines regulation in Australia, the key challenges faced, and the use of data analytics to improve its risk-based targeting of post-market compliance activities.

Cesar Compadre, Ph.D.

Professor

College of Pharmacy

University of Arkansas for Medical Sciences

Little Rock, AR

USA



Dr. Compadre is a professor at the Department of Pharmaceutical Sciences, of the University of Arkansas for Medical Sciences. He has extensive research experience on the development of bioactive compounds based on naturally occurring compounds, and on the use of molecular modeling in drug design and structure-activity studies. He has published over 90 papers and co-authored more than 70 patents related to the development of bioactive compounds.

He is also the developer of one FDA approved antimicrobial technology, which is commercially used, and he is also co-founder of Tocol Pharmaceuticals, a company focused on the development of enhanced vitamin-E analogues. Dr. Compadre has extensive International research collaborations in Drug Discovery, Global Health and Phytopharmaceuticals. Dr. Compadre has a BSPHarm degree, and obtained his Ph.D. degree in medicinal chemistry and pharmacognosy, from the University of Illinois at Chicago. He conducted postdoctoral research on structure-activity relationships studies using molecular modeling at the University of Illinois working with Dr. John M. Pezzuto and at Pomona College working with Professor Corwin Hansch. Additionally, he had a sabbatical experience at NASA Ames Research Center in computer modeling.

The Future of the “Botanical Drugs” Paradigm Requires Strong International Regulatory Harmonization

Most of the world depends on the use of products from nature to take care of their health needs. Products from nature have the benefit of being relatively inexpensive and usually have a tradition of use that made them readily accepted for many consumers. Unfortunately, many of the natural products in use lack the rigorous testing for safety and effectiveness like modern synthetic medicines go through. The United States Food and Drug Administration (FDA) has introduced “Botanical Drugs” as regulatory designation to include products containing vegetable matter marketed to diagnose, mitigate, treat, or cure a disease. This regulatory pathway offers a very promising opportunity to foster the development of safe and effective products that could be used world-wide. However, to fully realize the potential of Botanical Drugs, it is necessary to develop international harmonization protocols that allow the development of these products in a cost-effective basis.

Scott Crerar, Ph.D.

General Manager, Science and Risk Assessment
Food Standards Australia New Zealand
AUSTRALIA



Dr. Scott Crerar is General Manager of the Science and Risk Assessment Branch at Food Standards Australia New Zealand (FSANZ). This role is responsible for overseeing the scientific and risk assessment functions of the agency that includes biological sciences and genetically modified foods, chemical safety (toxicology) and nutrition, food data and analysis (food composition and dietary modelling), international and strategic science activities, and chemical residue related activities. Dr Crerar has worked in food safety and regulation for 20 years across a range of risk assessment roles including the public health assessment of agricultural and veterinary chemicals and risk assessment of chemical and microbiological hazards across a number of primary production sectors. Dr Crerar previously managed the FSANZ Science Strategy and the international activities including aspects relating to the APEC Food Safety Corporation Forum. Dr Crerar is a Veterinary Science Graduate and has post-graduate degrees in microbiology and epidemiology.

A New Framework for Regulatory Assessment of Novel Foods

The Australia New Zealand Food Standards Code (the Code) prohibits the sale of novel foods and the use of nutritive substances as ingredients or components of foods, unless permission is included in the Code. Definitions of nutritive substance and novel food are included in the Code to help identify the type of foods that are subject to pre-market assessment. However, it has become apparent that these definitions include terms that create uncertainty. Uncertainty creates difficulties for industry and food enforcement agencies in determining whether particular foods require permission in the Code before they can be added to, or sold as, foods. Therefore, Food Standards Australia New Zealand (FSANZ) is working on developing an improved framework for assessing and regulating nutritive substances and novel foods. This presentation will set out FSANZ's current thinking on a potential framework for the pre-market safety assessment of nutritive substances and foods new to the food supply. Specific focus will be applied to the risk assessment aspects of the properties of food or criteria that do not require pre-market assessment, those that may be appropriate for a lighter regulatory touch and foods that will still require a full regulatory assessment.

Valeriu Curtui, Ph.D

Head of the Nutrition Unit
European Food Safety Authority (EFSA)
ITALY, EU



Dr Valeriu Curtui is Head of the Nutrition Unit at the European Food Safety Authority (EFSA). His role is to manage the Unit in providing scientific and administrative support to the EFSA Scientific Panel on Nutrition, Novel Foods and Food Allergens (NDA Panel). The NDA Panel deals with questions related to human nutrition, foods for special groups and food allergies as well as associated subjects such as scientific substantiation of health claims and safety of novel foods. Valeriu joined EFSA in 2008 as a scientific officer working on chemical occurrence in food and dietary exposure and took up his current role in 2013. Prior to his employment with EFSA he was an academic at universities in Romania and Germany. He holds a PhD in Veterinary Medicine and his teaching and research activity focused on toxicology and chemical food safety.

Safety and Benefit Assessment of Food Supplements in the European Union

In the European Union (EU) food supplements are regulated as foodstuffs aimed at supplementing the normal diet of citizens with vitamins, minerals or other substances with a nutritional or physiological effect. EU legislation lays down a harmonized list of vitamins and minerals that may be added for nutritional purposes in foods and food supplements. The addition of substances other than vitamins and minerals is only partially harmonized in the EU.

There is no centralized approach for placing food supplements on the EU market, but EU Member States may require the food business operators to notify the placing on the market of a food supplement to the national competent authorities. The European Food Safety Authority (EFSA), at request of the European Commission (EC), provides scientific advice on the safety and bioavailability of new nutrient sources proposed by food business operators. Based on EFSA's advice, the EC may decide on the authorization of the nutrient source to be used in food supplements.

Where a substance other than vitamins or minerals is added to foods under conditions that would result in the ingestion of amounts of that substance greatly exceeding those reasonably expected under normal conditions and/or would otherwise represent a potential risk to consumers, EFSA may be requested by the EC to provide a safety assessment of that substance. Based on EFSA's assessment, EC may decide to include the substance in a list of substances whose use in foods in the EU is prohibited, restricted or under scrutiny.

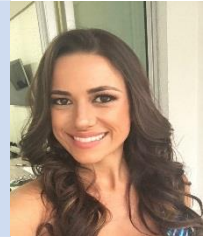
The EU legal framework provides a centralized approach for the assessment of claimed health benefits in Europe, with the benefit assessment carried out independently from the safety assessment. Health claims should only be authorized for use in the EU after a scientific assessment of the highest possible standard by EFSA. It is important to reiterate that a regulatory decision on the authorization of health claims is taken by the EC and the EU Member States and not by EFSA.

Stefani Faro de Novaes Ph.D.

Sanitary Regulation and Surveillance

Brazilian Health Regulatory Agency (ANVISA)

Brasilia, BRAZIL



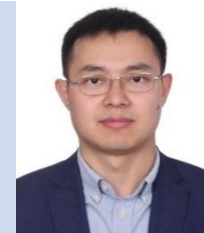
Dr. Stefani Faro de Novaes is a specialist in sanitary regulation and surveillance in the Brazilian Health Regulatory Agency (Anvisa). She holds a degree in Veterinary Medicine from Federal Fluminense University (2009), with professional experience in food safety. Master's degree in Veterinary Medicine in the Graduate Program in veterinary hygiene and technological processing of products of animal origin (2013). PhD in Veterinary Medicine in the same Graduate Program (2017). Member of the Brazilian delegation in *Codex Alimentarius*.

Food Supplements: Methodology used in the Brazilian regulation

Food supplements are a category of products characterized by heterogeneous composition, constant incorporation of technological innovations, strong advertising appeal, variety of claims and diversity in regulatory approaches. For many years, there was a fragmentation of Brazilian sanitary legislation since there was no provision for the category of food supplements. These products were divided into six distinct food categories (vitamin and mineral supplements, bioactive and probiotic substances, athlete's food, novel foods, foods with functional claim, food supplements for pregnant and lactating women) and one category of drugs, and they all had specific regulations. This regulatory gap promoted unnecessary barriers to marketing and innovation, making tough the sanitary control and risk management. To modernize the regulation of these products and simplify the regulatory stock, Anvisa performed a new regulation, which created the category of food supplement in Brazil. The methodology used considered the best regulatory practices to list all authorized safe ingredients for use in the composition of supplements. Nonetheless, all the approved claims were described with the specific usage criteria with the main goal of ensuring that supplements provide a significant amount of the substances and are effective. Anvisa considered the safety limits for each substance established by means scientific based risk assessment; the variation in the sensitivity of the different age groups; and the daily amount consumed of each substance from other food sources in Brazil. Other labeling requirements were established to reduce information asymmetry to consumers.

Xiaohui Fan, Ph.D.

Professor and Vice Dean
College of Pharmaceutical Sciences
Zhejiang University
Hangzhou, CHINA



Dr. Xiaohui Fan currently is professor and vice dean of College of Pharmaceutical Sciences at Zhejiang University, China. He also held an appointment of visiting professor of US FDA.

Dr. Fan received his Ph.D. in pharmaceutical sciences at Zhejiang University, China, in 2005. He did postdoctoral studies at the US FDA's National Center for Toxicological Research (NCTR/FDA) from 2005 to 2008, where his research focused on systems biology approaches to advancing regulatory science, especially in developing genomics data-based models to support regulatory decision-making. Thereafter, he was appointed as a faculty member by the College of Pharmaceutical Sciences at Zhejiang University. Research in his group includes both computational and experimental approaches, such as systems and network pharmacology, to advancing regulatory science of Chinese Medicine, emphasizing a 'systems-level' perspective.

Dr. Fan is reviewer and member of the editorial board for various scientific journals, and has published over 80 original papers and 4 book chapters.

Advancing Quality Control of Botanical Drugs using Computational Methods: A Case Study of *Panax Notoginseng*

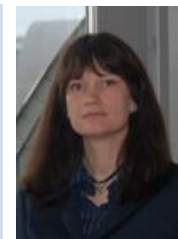
With tremendous expansion in the use of botanical drugs/herbal medicines worldwide, their quality has been an important concern for both health authorities and the public. Development of quality control methodology to ensure the safety and effectiveness of herbal medicines is greatly needed. *Panax notoginseng* is an important Chinese herbal medicine with a diverse medicinal application, such as anticarcinogenic and hepatoprotective effects and protecting cardiovascular and vascular system. Taking *Panax notoginseng* as a typical example, in a CDER Regulatory Science Research (RSR) funded project which is jointly conducted between US FDA's CDER, NCTR and Zhejiang University, various computational methodologies and analytical approaches were evaluated to distinguish different parts. The poster described this work entitled "Identification of the different root parts of *Panax notoginseng* by chemometric analyses: a comparative study" was selected for the first place award poster at FDA's Scientific Computing Day. We further proposed a computational method by integrating network pharmacology analysis and ingredient content to identify bioactive chemical markers (BCM) of *Panax notoginseng* for assessing the efficacy and consistency of different batches. As a result, notoginsenoside R1, ginsenoside Rg1, Re, Rb1 and Rd were identified as BCM of *Panax notoginseng* on treating cardiovascular and cerebrovascular diseases following an *in vivo* validation. These studies demonstrated the utility of computational methods to help assure the quality of the botanical raw materials and to support the safety and efficacy of the botanical drug products.

Gudrun Gallhoff, Ph.D.

Minister Counsellor

Health & Food in the Delegation of the European Union in Beijing

CHINA



Dr. Gudrun Gallhoff has been nominated Minister Counsellor for Health & Food in the Delegation of the European Union in Beijing, China as of 1 September 2018. Before her nomination she was deputy head of unit *Official Controls and Eradication of Diseases in Animals* in Directorate General Health and Consumer (DG SANTE) in Brussels, Belgium. She joined the European Commission in 1996. Since then she worked on pharmaceuticals, residues in food, general food law, cloning, food contact materials, food control and legal affairs.

She started her career as a veterinary practitioner in Germany. Here she also worked for a state laboratory, the federal ministry of health and a laboratory/consultancy enterprise.

Gudrun Gallhoff graduated from Hannover Veterinary College in 1985 and received her doctorate from the same institution in 1986. She moreover holds a Bachelor of Laws and a Master of Laws degree from British universities.

The Rules on Dietary Supplements in the EU

As an addition to a normal diet, food business operators market food supplements, which are concentrated sources of nutrients (or other substances) with a nutritional or physiological effect. Such food supplements can be marketed in “dose” form, such as pills, tablets, capsules, liquids in measured doses, etc.

There is a wide range of nutrients and other ingredients that might be present in food supplements including, but not limited to vitamins, minerals, amino acids, essential fatty acids, fibres, and various plants and herbal extract. Food supplements are regulated in the EU by Directive 2002/46/EC on the approximation of the laws of the Member States relating to food supplements.

The objective of the harmonised rules on those products is to protect consumers against potential health risks from those products and to ensure that they are not provided with misleading information.

With respect to the safety of food supplements, the Directive lays down a harmonised list of vitamins and minerals that may be added for nutritional purposes in food supplements (in **Annex I** to the Directive). **Annex II** of the Directive contains a list of permitted sources (vitamin and mineral substances) from which those vitamins and minerals may be manufactured. Only vitamins and minerals listed in Annex I, and in the forms listed in Annex II of Directive 2002/46, may be used for the manufacture of food supplements. This list has been amended to include additional substances.

The labelling, presentation, and advertising must not attribute the property of preventing, treating or curing a human disease to food supplements, or refer to such properties. Their label can bear health and/or nutritional claims, authorized in accordance with Regulation 1924/2006 on nutrition and health claims made on foods. Most of the food supplements bear health claims. Health claims imply that there is a relationship between a product and a health condition whereas nutritional claims state, suggest or imply that a food has particular nutritional properties.

In addition to the compulsory labelling requirements listed in the Regulation (EU) No 1169/2011, Directive 2002/46/EC requires some specific particulars for food supplements, as follows:

- the name under which food supplements are sold shall be 'food supplement'
- the names of the categories of nutrients or substances that characterize the product or an indication of the nature of those nutrients or substances;
- the portion of the product recommended for daily consumption;
- a warning not to exceed the stated recommended daily dose;
- a statement to the effect that food supplements should not be used as a substitute for a varied diet;
- a statement to the effect that the products should be stored out of the reach of young children.

The amount of the nutrients or substances with a nutritional or physiological effect present in the product shall be declared on the labelling in numerical form. The units used for vitamins and minerals shall be those specified in Annex I of Directive 2002/46. Information on vitamins and minerals shall also be expressed as a percentage of the reference values (%NRV) mentioned in the Annex XIII of Reg. (EU) No 1169/2011. Significant amounts should be taken into consideration.

Xingchao Geng, Ph.D.,

Professor

National Center for Safety Evaluation of Drugs (NCSED)

National Institutes for Food and Drug Control (NIFDC)

China Food and Drug Administration (CFDA), CHINA



Dr. Xingchao Geng received his bachelor and master degree from Peking University Health Science Center (Beijing, China) and Ph.D in pharmacology at The Fourth Military Medical University in China. He joined the National Center for Safety Evaluation of Drugs (NCSED), National Institutes for Food and Drug Control (NIFDC) for Toxicological Research to develop toxicological methods for safety evaluation of novel drugs in 2004. Currently, Xingchao Geng is deputy director of NCSED/NIFDC. He is excellent in pharmacology and new compound researching and discovery. He has more than twenty years experience in drugs screening and studying, especially in safety evaluation of drugs and has performed about 100 non-clinical drug safety assessment studies according to GLP regulations including 20 international studies from USA and France. He specializes in the research of new Biomarkers, immunotoxicity and hepatotoxicity research. He has published more than 50 papers and book chapters, and has been invited to present in national and international conferences. AS a visiting scholar, He worked and was trained in Huntingdon life Sciences company in United Kingdom, National Toxicology Research Center (NCTR) of US FDA, the United States Environmental Protection Agency (EPA) and National Institute of Environmental Health Sciences (NIEHS), *et al.*

New Approaches and Special Consideration for Non-Clinical Safety Assessment of Herbal Medicines

There are more than ten thousands of herbal medicines widely used in China according to the document. However, most herbals using in clinic are lack of sufficient preclinical safety data. In recent years, with the increase of serious adverse reactions reports, the safety of herbal medicines received more and more attention in public. Lots of herbal medicines were re-evaluated to reduce and control the toxicity risk. There are still some difficulties and problems to be faced and considered in herbals non-clinical evaluation. Herbals usually have thousands of complex components, and complex toxicity mechanisms, comprehensive effects with multiple target effects, . Some components for quality control have nothing to do with the toxic effect. There are big differences in components for quality control among different herbals. There are also lots of differences in effects components and toxicity components among different batches and different places of production. In addition, some non-standard processing methods, pesticide residues and heavy metals will also affect the safety evaluation of herbal medicines. Recently, many seemingly safe herbal medicines, such as *polygonum multiflorum*, *pseudo-ginseng*, *epimedium*, *evodia rutaecarpa*, etc., have been reported a large number of clinical adverse reactions. NIFDC carried out some investigations on the causes of these adverse reactions. For example, we studied the toxic constituents derived from *polygonum multiflorum* which might cause liver injury and explored the preliminary mechanism of *polygonum multiflorum* induced liver injury. Cell cycle, cell apoptosis, high-content screening assay, two dimension electrophoresis and validation with molecular biology techniques were investigated thoroughly on HepaRG cell line at different doses at different times. Basic researches and systematic researches of herbal medicines need to be further strengthened, early assessment technologies and safety database of herbal medicines might be the focus areas in the future.

Takashi Hakamatsuka, Ph.D.

Head, Division of Pharmacognosy, Phytochemistry and Narcotics
National Institute of Health Sciences
JAPAN



Dr. Takashi Hakamatsuka is Head of Division of Pharmacognosy, Phytochemistry and Narcotics at National Institute of Health Sciences (NIHS). The institute conducts testing, research, and studies toward the proper evaluation of the quality, safety, and efficacy of pharmaceutical products, foods, and the numerous chemicals in the living environment. And his division mainly engages in research for evaluation and standardization of herbal medicines to ensure their quality, efficacy and safety and for development of analytical method of narcotics, stimulants and other abused drugs. Additionally, he is the Chairman of Japanese Pharmacopoeia Expert Committee on Crude Drugs.

Dr. Hakamatsuka received his Ph. D in pharmaceutical sciences at the University of Tokyo and he began his career in the Faculty of Pharmaceutical Sciences, the University of Tokyo as a research assistant of natural product chemistry in 1989. He moved to the Faculty of Pharmaceutical Sciences, Tokyo University of Science as a lecturer of Phytochemistry in 1995. And he joined NIHS as a section chief of Division of Pharmacognosy, Phytochemistry and Narcotics in 2005 and was promoted to the division head in 2013.

Recent Progress in Approval Systems for Herbal Medicines in Japan

Most herbal medicines in Japan are based on Japanese traditional medicine, Kampo medicine. Currently, 148 ethical Kampo formulations (Kampo prescription drugs) are registered in the National Health Insurance price list and Kampo medical care can be given within the national insurance system, which shows that Kampo medicine is a part of conventional medicine in Japan. Japan has a unitary license system, namely, medical doctors and pharmacists educated by Western medicine can only use Kampo drugs. Japan also has a unified drug approval system that never distinguish between Western and Kampo drugs, and both types of drugs are subjected to the same regulations, which make development of new Kampo prescription drugs difficult. To facilitate the development of Kampo prescription drugs, the specific guideline for the approval of new drugs of herbal origin should be required. On the other hand, approval standards have been established for OTC drugs in order to rationalize the OTC drug approval process and increase its transparency. The criteria of these approval standards include concrete requirements related to active ingredients, their contents, dosage and administration, indication, etc. The presentation will describe the current situation of the approval system for prescription and OTC drugs of herbal origin in Japan.

Marta Hugas, BSc, MSc, Ph.D.
Chief Scientist
European Food Safety Authority (EFSA)
ITALY, EU



Dr Marta Hugas is serving as Chief Scientist at the European Food Safety Authority. This position addresses the development of EFSA's scientific strategic direction; acting as focal point on scientific matters and facilitating the understanding of science; fostering scientific cooperation as well as leveraging connections and networks for promoting EFSA's research priorities. She joined EFSA in 2003 and since then Marta has held several positions: Head of Biological Hazards Unit (BIOHAZ), Head of the Risk Assessment and Scientific Assistance Department a.i. (RASA) and Head of the Biological Hazards and Contaminants Unit (BIOCONTAM).

Marta holds a BSc in biological sciences, an MSc in genetics and microbial biotechnology and a PhD in food microbiology. Prior to joining EFSA, she worked for the Institute for Food and Agricultural Research and Technology (IRTA) in Spain, where she was Head of the Food Microbiology and Biotechnology Unit and led a research group on applied research on meat and food safety. From 1992 to 2004 she was an Associate Professor at the University of Barcelona. Marta's areas of expertise focus on: food hygiene, development of starter and bio protective cultures, probiotics for the safety of poultry meat, emerging preservation technologies as well as risk assessment of biological hazards. Dr Hugas has extensively published papers and book chapters.

The European Food Safety Authority's Approach on Data for Safety and Benefit Assessment in the Area of Food Supplements

In the context of authorisation of a new nutrient source or a claimed health benefit of a food/food supplement, applicants have the duty to provide all the available scientific data that are pertinent for the safety and for the benefit assessment, respectively. As such, applications should be comprehensive and complete in line with the requirements listed in the applicable EFSA guidance documents. EFSA may search for additional information, especially regarding the safety of such substances. When EFSA is requested to assess the safety of a substance present in food supplements already on the EU market, EFSA may launch ad hoc calls for data to retrieve all relevant information from interested parties to be used for the evaluation of the substance. Within the risk assessment process, it might be necessary to estimate the exposure to certain substances present in food supplements. With this aim different information can be used by EFSA in addition to those provided by the applicant. In particular, the EFSA Comprehensive European Food Consumption Database provides information on the consumption of food and beverages, including food supplements, in different EU countries and age groups. This innovative database is particularly useful when the proposed dose for the supplement is not available and/or when the substances under evaluation are as well present in foods other than supplements. The availability of detailed, harmonised and high-quality food consumption data for use in dietary exposure assessments is one of EFSA's priorities. To this end, and since 2005, EFSA has been working in close cooperation with all organisations operating in the field towards i) harmonising dietary survey methodologies and; ii) building of a common European Union food consumption database within the EU Menu framework project.

Information from labelling may also be used by EFSA within the risk assessment process. Since 2016, EFSA got access to the Mintel's Global New Products Database which contains labelling information on more than 60,000 dietary supplements of which more than 20,000 are or have been available on the European food market.

For the substantiation of a health claim, the application dossier must include data on the characterisation of the food or food constituent for which the claim is made, information to allow the characterisation of the claimed effect, and published and unpublished data to substantiate the health claim.

Ikhlas A. Khan, Ph.D.

Director

National Center for Natural Products Research

University of Mississippi

University, MS, USA



Dr. Ikhlas Khan is the Director of the National Center for Natural Products Research, Director of the FDA Center of Excellence, Research Professor, as well as Professor in the Department of Pharmacognosy at the National Center for Natural Products Research at the University of Mississippi. Additionally, he is the Director for Sino-US TCM Research Center; Director, Center for Research of Indian Systems of Medicine (CRISM); Research Professor and Coordinator for Natural Products Research Center for Water and Wetlands Research; a visiting Professor at Hunan University of Chinese Medicine, China; an Adjunct Professor, Chinese University of Hong Kong; visiting professor for King Saud University, Saudi Arabia since 2010; Soochow University, since 2010 and Heilongjiang University of Chinese Medicine, The People's Republic of China since 2010. He received a D. Litt (Honoris Causa) from University of Hamdard, Delhi, India 2012; a B.S. in Chemistry in 1980 and a M.S. in Organic Chemistry in 1982 from the Aligarh Muslim University in Aligarh, India. Dr. Khan then received a Ph.D. in Pharmacy from the Institute fuer Pharmaceutische Biologie in Munich, West Germany in 1987 and postdoctoral studies at Swiss Federal Institute of Technology (ETH) Zurich. After completing his education, Dr. Khan began his career with the University of Mississippi in 1992 as a research scientist. He became a Research Assistant Professor in 1995, and was promoted to Research Associate Professor and Director of the FDA program in 2001, Assistant Director of NCNPR in Oct. 2002, Professor in July 2005, to Associate Director in 2015 and most recently to Director in 2017.

Dr. Khan's primary research interests include analytical fingerprinting for standardization of herbal products, and bio-analytical approaches to improvement of product quality and safety.

Dr. Khan has authored or co-authored over 700 original research articles, publications, or reviews. He has been an invited speaker at numerous events. Dr. Khan serves as reviewer for several journals.

Dr. Khan is the recipient of numerous awards, including: most recently he was awarded "University of Mississippi's Distinguished Professor, 2018"; "The Wiley Award, Association of Official Agricultural Chemists International, 2018"; "Qihuang International Prize of China Association of Chinese Medicine, 2017"; "Outstanding Contributions in TCM Analysis & Quality Standards, 2017"; "Mark Blumenthal Herbal Community Builder Award, 2017"; "Cumberland Pharmaceuticals, Inc. Research Award, 2016", "UM Distinguished Researcher Award, 2016", "IASTAM Zandu International Award for Excellence in Field of Ayurvedic and/or Natural Products", 2015, "Outstanding Contribution in Natural Product Research", Water's Corporation, given at the ICSB 2013, "The Center for Food Safety and Applied Nutrition" (CFSAN) Director's Special Citation Award, 2012; the Varro E. Tyler Prize, the American Society of Pharmacognosy, 2011; the Nutrition Business Journal Education Award, 2011; and many more.

Dr. Khan serves on several committees of National Center for Complementary and Alternative Medicines, Washington, D.C. which include serving as Invited Reviewer and as a Committee Member of the Product Quality Working Group. Additional appointments to national and/or international committees include membership of the First Editorial Board of World Journal of Traditional Chinese Medicine (WJTCM); membership of expert panel of United States of Pharmacopoeia (USP) Committee; Advisory Board of Women's Health & Asian Traditional Medicine (WHAT); Advisory Board of American Herbal Product Association, Washington, D.C.; Committee of AOAC Dietary Supplement Task Force.

Memberships to scientific organizations include fellowship of the American Institute of Chemists (FAIC); fellowship of the Royal Society of Chemists (FRSC); member of the International Society for Ethnopharmacology; member of the American

Chemical Society; the Society of Medicinal Plant Research; The American Association for the Advancement of Sciences, and the New York Academy of Sciences, American Association of Pharmaceutical Scientists, International Society for Horticultural Science, National Advisory Council for Complementary and Alternative Medicine, American Society for Clinical Pharmacology and Therapeutics, and the American Association for the Advancement of Science. He is a member of the American Society of Pharmacognosy, where he served as Chair of the Constitution of By-laws Committee in 1998. He also served as a WHO consultant in Vietnam in 2002. He is an honorary memberships of Sigma Xi, the Scientific Research Society; Rho Chi, the Pharmaceutical Honor Society.

A Need for Comprehensive Approach to Assess the Quality and Safety of Botanicals/Dietary Supplements

While the research is focusing on determining the beneficial effect of traditional medicines, it is becoming obvious that the identity and authentication issues have to be resolved, which requires a multidisciplinary effort. There are only few well identified and characterized plants extract available in the market but the majority of the products are not. The same time new botanicals are being introduced in the market where there is little or no information available on chemistry and pharmacology. On the other hand some botanicals are well characterized but other possible adulterants are not well studied.

Analytical tools can be applied to measure the exact amount of a particular marker/biomarker compound but in most cases, it does not resolve the question of identity of the plant. Since a single approach will not be adequate to address the unambiguous identity of a botanical, the NCNPR is undertaking a comprehensive approach utilizing morphological/ anatomical/ genetics and chemical analysis methods, to address this issue.

Jong Kwon Lee, D.V.M., Ph.D.

Director, Toxicological Research Division
National Institute of Food and Drug Safety Evaluation (NIFDS)
Ministry of Food and Drug Safety (MFDS)
KOREA



Dr. Jong Kwon Lee is the director of Toxicological Research Division at National Institute of Food and Drug Safety Evaluation (NIFDS), Ministry of Food and Drug Safety (MFDS). He received his Ph.D. in the college of Veterinary Medicine, Seoul National University. He started his career as a scientific officer in NIFDS, where he has been since 1991. He worked as a visiting fellow in US National Institute of Environmental Health Sciences (NIEHS) from 2008 to 2010. He serves as ICH (International Conference on Harmonisation) S1 (Carcinogenicity) Korean delegate and as OECD WNT National Coordinator of Korea. He is a Korean board-certified toxicopathologist.

Safety Assessment of Dietary Supplements Containing Medicinal Herbs in Korea

Korea Ministry of Food and Drug Safety (MFDS), the umbrella organization of NIFDS, enacted the “Functional Foods Act” to set criteria for manufacturing, production, import, distribution and preservation of functional food products (or dietary supplements) in 2002. Standards and specification were established for each functional ingredient and product to secure consumer safety. To obtain individual recognition as a functional ingredient, manufacturers (or importers) should submit the data to prove safety and functionality, and the submitted data would be reviewed and approved under Article 14 “Recognition of raw materials, etc.”

NIFDS has been running Korea National Toxicology Program (KNTF) since 2002, which includes toxicity tests and toxicological studies to support food and drug safety evaluation and management. One of the KNTF main projects is toxicity tests on medicinal herbs, because most herbs are lack of toxicological information. About fifty medicinal herbs were studied on single dose toxicity, 90 days repeated dose toxicity and genotoxicity.

As functional foods market grows, various hazardous factors are increasing such as adulteration with harmful substances. In 2014, a herb adulteration scandal had hit our country in the market of dietary supplements. *Cynanchum wilfordii* Hemsley, a long-time used medicinal herb, has been used as an ingredient of dietary supplements. *Cynanchum auriculatum* Royle ex Wight is not a medicinal herb, but its appearance is very similar to *Cynanchum wilfordii* Hemsley and so it was adulterated in the dietary supplements. The toxicity studies on *Cynanchum wilfordii* Hemsley and *Cynanchum auriculatum* Royle ex Wight were carried out. The risk assessment of them performed for safety concern.

Bo Li, Ph.D.

Institute for Food Control
National Institutes for Food and Drug Control (NIFDC)
Beijing, CHINA



Dr. Bo Li has worked in the Department of Food Risk Assessment, Institute for Food and Cosmetic Control, National Institutes for Food and Drug Control as an associate professor since 2009. He received his PhD from the Department of Immunology, School of Basic Medical Sciences, Peking University Health Science Center in 2003. He then pursued postdoctoral training in immunology at the Department of Microbiology and Immunology, Dalhousie University, Canada from 2004 to 2007. He worked in the Department of Immunology, School of Basic medical Sciences, Capital Medical University as an associate professor from 2007 to 2010. His research interests include mast cell signaling mechanisms in allergy, assessment of function and safety of health food & new food raw materials and food policy reform. His studies demonstrated a clear role for the newly synthesized immediate early gene early growth response factor 1 (Egr-1) in FcεRI-induced TNF and IL-13 production by mast cells. In addition, Egr-1 is required for stem cell factor-induced IL-13 expression, but not mast cell growth, it suggested that Egr-1 represented a novel mechanism for SCF-induced mast cell activation. Some works were published in the Journal of Biological Chemistry, Blood. In recent years, he has participated in the revision of the food safety law and the health food regulatory policy in China.

Challenges and Strategies for Safety Assessment of Health Food in China

In April 2015, China promulgated the Food Safety Law of the P. R. China (Revision), in February 2016, China Food and Drug Administration (CFDA) issued the Measures for the Administration of the Registration and Filing of Health Food. Based on the new food control system, the health food supervision system has been adjusted to a combination of registration and filing system from only registration. According health food registration system, a health food cannot be sold without the approval of the government. For filing health food, a company can legally sale their health food in the market after they recorded all information of health food in the governmental health food filing system. It is a huge challenge to ensure health food's safety and function in the health food registration and filing system in China. In order to improve the health food safety level continuously, firstly, CFDA is going to set up directories of raw material and function of health food, respectively. The directory will include the name, function, dosage of raw material of health food. The application of raw materials in filing health food production will be strictly limited. Secondly, the CFDA will strengthen to sample and test for health food in the market. Thirdly, the CFDA will strengthen the on-site inspection for health food enterprises.

Jing Li, Ph.D.

Botanical Review Team (BRT) of Office of Scientific Quality
Center for Drug Evaluation and Research (CDER)
Food and Drug Administration (FDA)
Silver Spring, MD, USA



Dr. Jing Li conducts pharmacognosy review in the Botanical Review Team, Scientific Staff, Office of Pharmaceutical Quality, Center for Drug Evaluation and Research, at US Food and Drug Administration (BRT/SS/OPQ/CDER/US FDA). She has reviewed numerous new botanical drug applications for a wide variety of therapeutic areas. In addition, she is responsible for 503A compounding review, regulatory related consults, and generic drug review. She is a CDER/FDA liaison serving on USP 2015–2020 Botanical Dietary Supplements and Herbal Medicines Expert Committee, USP 2015–2020 Botanical Dietary Supplements and Herbal Medicines Nomenclature Committee, and Board member of PDQ Integrative, Alternative, and Complementary Therapies Editorial Board, NCI/NIH.

Jing holds a B.S. in Pharmacy (Beijing University of Chinese Medicine), M.S. in Pharmacognosy (Chinese Academy of Medical Sciences & Peking Union Medical College), and Ph.D. in Pharmacognosy from The University of Mississippi. She had more than 10 years of working experience in exploring new drugs from herbal medicines in China and many years of review and regulatory experience in TCM and western medicine in Center of Drug Evaluation (CDE), Chinese Food and Drug Administration (CFDA), where she was the Deputy Director of Office of Import Drug in CDE/CFDA.

She conducted systematic postdoc training in natural product chemistry and pharmacology at the University of Texas Health Science Center at San Antonio, where she discovered a new class of microtubule stabilizing agents from plant *Tacca* with higher potencies and less drug resistance than paclitaxel both *in vitro* and *in vivo*. She has published 25 peer-reviewed articles, reviews and book chapters and holds 2 patents on new classes of microtubule targeting agents.

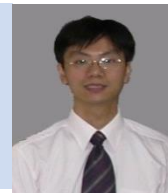
Development of Botanicals as New Drugs: Revised Guidance and Review Experience from US FDA

In the United States, botanical products can be classified into several regulatory categories under the Federal Food, Drug, and Cosmetic Act (FD&C Act), such as foods, dietary supplements, cosmetics, or drugs, based on the claimed "intended use" of those products. Each category may have different regulatory requirements. For example, botanical products with structure or function claims are regulated by the Center for Food Safety and Applied Nutrition (CFSAN) at FDA as either foods, dietary supplements, or cosmetics that require only limited premarket review of new ingredients and no pre-market approval of products. However, if botanical products are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans, they are subjected to regulation as drugs. FDA's Center for Drug Evaluation and Research (CDER) reviews Investigational New Drug Applications (INDs) and New Drug Applications (NDAs), which includes assessment of pharmacognosy, chemistry manufacturing and controls (CMC), and safety and efficacy data from non-clinical and clinical studies.

From 2002 to 2017, FDA received over 700 botanical pre-IND meeting requests, INDs, and NDAs. During that time, two botanical drugs have been approved, including Veregen® in 2006 and Mytesi® in 2012. The first botanical drug products guidance, Guidance for Industry-Botanical Drug Products, was published in draft form in 2000 and finalized in 2004. With accumulated knowledge and regulatory experience on botanical drug product development, FDA published a revised Botanical Drug Development-Guidance for Industry in December 2016, with the new sections added to address late-phase development and NDA submission to facilitate botanical drug product development. This talk will provide an overview of botanical drug product development and regulations in the US and will highlight our current thinking and review mechanisms for the review of these products.

Qionglin Liang Ph.D.

Director of Modern Research Center of Traditional Chinese Medicine
Co-Chair of Department of Chemistry, Tsinghua University)
CHINA



Dr. Qionglin Liang serves as the Director of Modern Research Center of Traditional Chinese Medicine, and Co-Chair of Department of Chemistry, Tsinghua University. He got his Sc.B and Ph.D at Department of Chemistry, Tsinghua University successively in 2000 and 2005 respectively, and then was appointed here as assistant professor, tenured associate professor and Principal Investigator. His research interests focused on bio-analytical technologies and devices and their applications in biomedical and pharmaceutical science, supported by Education Ministry's New Century Excellent Talents Supporting Plan and several national major programs (NSFC, MOST, MOE). He has published over 150 peer-reviewed papers in high-impact journals such as *Adv. Mater.*, *Adv. Science*, *PNAS*, *Cell*, *Anal Chem* and *Lab chip*, with over 3000 citations, claimed over 20 Chinese invention patents and 2 EU patents, co-authored five monographs and have also shared thrice of National Scientific and Technological Advance Prize. He has been elected as the Chair of the Committee of Young Scientists of Beijing Physical & Chemistry Testing Technology Society, the Vice Chair of the Committee of Young Scientists of China Association of Instrumental Analysis(CAIA), the secretary and member of executive panel of Chinese Biopharmaceutical Technology Association (CBTA) and Vice Chair of New Product Development Committee of China Association of Traditional Chinese Medicine (CATCM).

Emerging Technologies for the Quality Control and Activity Screening of Chinese Herbal Medicine

Traditional Chinese medicines (TCM) or Chinese Herbal Medicines are well-known for their clinical efficacy, experiences, and resources, and deemed as a valuable medicinal repository. The quality control of TCM remains challenges due to its complexity and requires a major breakthrough in methodologies and technologies. This presentation is to give a mini-review of recent advances of TCM quality control and activity screening. The comprehensive characterization of TCM also requires an appropriate technique platform, for that we had proposal of combination of chromatographic fingerprint and the assay of multi-index-component of TCM based on the chromatography and coupling techniques, especially the combination of chromatography/Mass spectrometry. Our research group contributed to the development of TCM fingerprint technologies such as the Functional Chromatographic fingerprint of TCM, Multi-wavelength and Multi-index-components Chromatographic fingerprint of TCM, 2D-chromatography (HPLC X UPLC) fingerprint, online NIRS fingerprint and establishment of fingerprint database.

Besides of the development of chemical fingerprint, we also introduce the global systems biology and omics technologies such as genomics, proteomics and metabolomics to the development of bio-response fingerprint, and apply these technologies for the TCM quality evaluation, quality control as well as R&D of new composite medicines. As one of Emerging Technologies, lab on a chip which means a kind of microfluidics-based micro-device has exhibited great potential in pharmaceutical analysis and pharmacological activity screening. In this presentation I'd like to report our recent advance in the study of microfluidics-based single cell analysis, metabolomic analysis, and organ biomimic analysis. We proposed a strategy of subcellular metabolomics based on chip-MS and provided a platform for the study of subcellular metabolome and metabolic flow between the mitochondria and the cytoplasm, for example, mitochondrial metabolomic analysis has been conducted for the investigation of the protective effect of nicotinamide towards cardiomyoblasts hypoxia/re-oxygenation injury. For the aspect of organ biomimic analysis, we mainly focused on cardiovascular model such as angiogenesis on a chip and myogenesis on a chip, and also we'd like present our recent work in flexible fabrication of various structures of hydrogel microfibers and their application in biological or pharmaceutical researches.

Chang Liu, Ph.D.

Institute of Medicinal Plant Development
Chinese Academy of Medical Science
CHINA



Dr. Chang Liu is currently Associate Director of Bioinformatics in Institute of Medicinal Plant Development (IMPLAD) affiliated with Chinese Academy of Medical Science (CAMS) in Beijing, China. Professor Liu is a graduate from University of Minnesota (Twin Cities Campus) with a Ph.D degree in Pathology and a Master degree in Computer Science. After graduation, he has worked in GlaxoSmithKline Corp (RTP, NC), Yale University, University of Hongkong, until now, IMPLAD of CAMS. Prof Liu has published more than forty research papers on Journals including Nature Communication, Science, PNAS and etc. He has been awarded the 1st prize for Science and Technology Development from Minister of Science and Technology of China and Association of Traditional Chinese Medicines in 2014 and 2015 for the Development of A DNA Barcoding based Medicinal Plant Molecular Identification System. He is an expert in plant genomics and is the organizer of the “1000 Medicinal Plant Genome Plan” sponsored by CAMS and Illumina Corp.

Establish Genomic Reference for Chinese Herbal Medicine Towards Health Food Safety

Precise determination of the sources of bioproducts is of critical importance in ensuring the safety and efficacy (if relevant) of general food, health food and traditional medicinal products. DNA barcoding technology, as a standardized molecular identification technology, has been fully developed and widely used in the food and medicinal industries in China. However, the focus on a few barcode markers leads to the difficulty in the differentiation of closely related species and subspecies. He we have developed several resources for the determination of sources in the mixture of biomaterials, most notably, health food and traditional medicinal products. Firstly, together with Illumina, we are building the world’s most comprehensive medicinal plant genome database; Secondly, we have developed several computer algorithms. The sourceIDNGS can use reads generated from the Next Generation DNA Sequencing Technology for direct species determination. The seqDivGap can be used to identify markers for the differentiation of closely related species; Finally, we have set up a blockchain that can be use to trace the bioproducts from seed banks to consumers. Taking together, these technologies will greatly improve our ability to control the safety and efficacy of bioproducts such as health food and traditional medicines.

Changxiao Liu, Ph.D.

Tianjin Institute of Pharmaceutical Research
Tianjin Binhai Center for Food and Drug Regulatory Science
CHINA



Dr. Liu Changxiao, researcher, professor, doctoral supervisor. In 1992, Liu received the special allowance of the state council and was elected academician of Chinese academy of engineering in 2003. Now Liu is Honorary President of the Tianjin Institute of Pharmaceutical Research (TIPR) and Director of TIPR academic committee, director of state key laboratory of drug release technology and pharmacokinetics at TIPR, a member of the national pharmacopoeia committee advisory committee, deputy director of expert committee of CFDA generics committee, a member of expert committee, Chinese Study society for Drug regulatory Science(CSSDRS), the Presidents of Tianjin pharmacological society, Tianjin pharmaceutical society and Tianjin Society Committee, and director of the China office of ISSX. From 1990 to 20012, Liu was member of Former national new drug research and development of the expert committee, the national GLP expert committee, national science and technology, economic experts committee, national new drug evaluation committee, the Chinese pharmacological society executive director and deputy director, the Chinese pharmacological society drug metabolism, director of the professional committee members, and other social functions.

Development of Regulatory Science in China

Regulatory Science is a new discipline that has been developing rapidly in the past 10 years. How to promote Regulatory Science to improve the efficiency and supervision of innovative drug development is an important area of development which has been of great concern to the Chinese government, academia and industry in recent years.

Reviewing the development of China's regulatory science in recent years, the main advances are as follows: (1) Establish special research organization, planning accord with the characteristics of China's drug development research direction, in 2012, Tianjin Institute of Pharmaceutical Research (TJIPR) establish cooperation relationship with the FDA toxicology research center(NTRC), in 2013 established the first domestic regulatory science research center, Tianjin Binhai Center for Food and Drug Regulatory Science. In 2017, under the guidance of the CFDA cooperation, Tsinghua University established a drug regulatory science research institute in 2018. (2) The establishment of Chinese Drug Regulatory Science Research Association (CDRSRA) and regional (such as Shanghai and Tianjin) research associations, as Nongovernmental organization (NGO), provided the public platform for carrying out relevant academic exchange activities. The CDRSRA was established in 2013 and held two national regulatory science conferences in 2015 and 2017, respectively. (3) As the national think tank and academic advisory organization of the country's highest engineering science and technology, the Chinese academy of engineering (CAE) has set up an advisory research project on the strategic development of drug regulatory science in 2015. (4) Development of Herb medicine quality regulation is based on the challenges of quality assessment, the current status of quality and process controls from raw materials to herbal medicinal products listed in Pharmacopoeia were analyzed and the research models including discovery and identification of Q-markers, analysis and quality management of risk evaluation were designed. We introduced a few new technologies and methodologies, such as DNA barcoding, chromatographic technologies, fingerprint analysis, chemical markers, bio-responses, risk management and solution for quality process control. The quality and process control models for herbal medicinal products were proposed and the transitivity and traceability system from raw materials to the finished products was constructed to improve the herbal quality from the entire supply and production chain. The subject is the development of innovation herb quality evaluation method and technology to provide reference for China government and regulators.

Nan Mei, Ph.D.

National Center for Toxicological Research
US Food and Drug Administration (FDA)
Arkansas, USA



Dr. Nan Mei is a Research Biologist in the Division of Genetic and Molecular Toxicology at the U.S. FDA's National Center for Toxicological Research (NCTR). He graduated from Hebei Medical University (China) in 1984 and received his Ph.D. from the University of Occupational and Environmental Health (Japan) in 1997. He worked as a postdoctoral fellow in the Department of Experimental Oncology, Cross Cancer Institute (Canada) from 1998 to 2001, and then joined the FDA/NCTR in 2002. His completed and on-going projects include the evaluation of the mutagenic effects of direct mutagens, herbal dietary supplements, industrial compounds, nanoparticles, ingredients in cosmetics and other retail products, and tobacco products. Dr. Mei has published 92 peer-reviewed research articles in scientific journals and 12 book chapters. He has given 32 oral presentations at national/international scientific meetings.

Toxicological Evaluation of Dietary Supplements Using Emerging and Conventional Methodologies

The uses of herbal dietary supplements are rapidly growing worldwide, with increased recognition for the need to improve individuals' health. However, evidence of carcinogenicity in several popular herbal extracts, from multiple U.S. National Toxicology Program two-year rodent studies, has raised concerns about their safeties. Recently, numerous herbal products have been classified as possible human carcinogens (Group 2B) by the International Agency for Research on Cancer (IARC). It is challenging to evaluate dietary supplements' efficacies and safeties due to the complexities of the herbs' chemical natures. In general, there is a need for better understanding of dietary supplements' risk and efficacy profiles due to a lack of comprehensive toxicity data. The integration of traditional toxicological approaches with high-throughput molecular profiling technologies provides new approaches to investigate alterations in gene/protein activities and biological pathways/functions that respond to xenobiotic compounds in animals and humans. In addition, the combination of *in silico* tools and conventional methodologies can help us better understand the toxicological effects of dietary supplements. We have performed several studies to evaluate herbal dietary supplements and their constituents, and we will provide examples of how emerging and conventional approaches were implemented to evaluate the safety and toxicity of dietary supplements in this presentation.

Latasha A. Robinson, M.S.

US Food and Drug Administration (FDA)
China Office
USA



Latasha A. Robinson is currently the International Relations Specialist for Food and Feed for the United States Food and Drug Administration, China Office. Prior to joining her current office, she was the Chief of the Dietary Supplement and Labeling Compliance Branch, within the within the US Food & Drug Administration's, Center for Food Safety & Applied Nutrition (CFSAN), Office of Compliance, where she oversaw a staff of individuals who were responsible for the implementation of enforcement programs for, dietary supplements (GMP's, NDIs, labeling, product claims and safety), nutrition labeling, food and color additives, infant formula, medical foods and cosmetics.

Before coming to the US Food & Drug Administration, Latasha previously worked as a System Safety Engineer for the United States Navy - Naval Surface Warfare Center in Dahlgren, VA, where she ensured the biological and chemical safety of Navy combat ships. Latasha holds a Bachelor's of Science Degree in Biology from Howard University in Washington, DC, and a Master's of Science in Regulatory Science with a concentration in drugs and biologics from the University of Maryland, School of Pharmacy in Baltimore, Maryland.

Dietary Supplement vs Drug

Health Foods, Dietary Supplements, Food Supplements, these products are known by various names around the world. This presentation will explain the definition of a dietary supplement as recognized by the US Food and Drug Administration.

Steven G. Rozen Ph.D.

Director, Duke-NUS Centre for Computational Biology
Associate Dean of Research Informatics
Professor of Cancer & Stem Cell Biology
Duke-NUS Medical School, SINGAPORE



Dr. Steve Rozen's research has ranged over bioinformatics, human genetics & cancer genomics. Rozen founded and directs the Duke-NUS Centre for Computational Biology. The Centre's faculty has published > 140 scientific papers since 2011 and the Centre offers a PhD program in bioinformatics. Rozen's own laboratory now focuses on bioinformatics and cancer genomics, and is part of a team-science effort in cancer genomics that has led to multiple papers, including 5 in Nature Genetics. This research was also recognized by the American Association for Cancer Research (AACR) 2018 Team Science Award for work on aristolochic acid mutagenesis in liver and urinary tract cancers and for genomic studies of biliary tract cancers, lymphomas, and gastric cancers. Within cancer genomics, the Rozen Lab studies alternative splicing, lncRNAs, and the use of mutational signatures as tools for studying the molecular epidemiology of cancer. Rozen also created and maintains the widely-used Primer3 software for PCR primer design. Previously, he also worked extensively on identifying mutations in human Y chromosomes and on their clinical consequences, as reported in multiple publications in Nature Genetics and Nature.

Mutational Signature Analysis for Molecular Cancer Epidemiology: The Example of Aristolochic Acid

Widely varying rates of different cancer types across space and time provide prima facie evidence that environment strongly influences cancer risk. Mutagenesis is a major cause of cancer, and cancer genomes are affected by mutations as part of oncogenesis. There are unmet needs for improved mutagenicity testing (ie, safety testing) and for improved assessment of the roles that specific mutagens play in causing cancer. Inexpensive genome sequencing has created novel opportunities to meet these unmet needs with (1) improved in-vitro testing of compounds' mutagenicity and safety and determination of their characteristic mutation signatures and (2) substantially improved understanding of the roles of mutagens in cancer risk and of the molecular epidemiology of cancer – improved understanding of the role of mutagenic exposures in explaining variation in cancer incidence across space and time. Mutational signatures can point to mutagenic exposures that elevate cancer risk. These in turn can point to opportunities for primary prevention through regulation and education, and secondary prevention through enhanced screening of exposed individuals. Mutational signature analysis requires a confluence of laboratory and computational approaches. I will review the state-of-the art of mutational signature analysis and present the case of aristolochic acid in depth. Until recently, we thought that aristolochic acid mainly caused urinary tract tumors in a few geographical hot spots. However, our and others' work now also implicates aristolochic acid mutagenesis in liver and bile duct cancers throughout East Asia, and in one area nearly 80% of liver cancers have mutations due to AA.

Nandakumara D Sarma, RPh, PhD.

Director, Dietary Supplements and Herbal Medicines
United States Pharmacopeia
Rockville, MD, 20852
USA



Dr. Nandakumara (Nandu) Sarma is the Director for the Dietary Supplements and Herbal Medicines program at US Pharmacopeia (USP) responsible for strategy and external stakeholder engagement for new and innovative projects, working with global stakeholders and expert volunteers in the development of quality standards (monographs and general chapters) for dietary supplements and herbal medicines that are published in the USP *Dietary Supplements Compendium* (<http://www.usp.org/dietary-supplements/overview>) and the *Herbal Medicine Compendium* (<http://hmc.usp.org/>).

Before joining USP 2006, he was a post-doctoral fellow at National Cancer Institute, Bethesda, and Thomas Jefferson University, Philadelphia and was a Senior Scientific Officer at The Himalaya Drug Company, India. His research experience includes isolation and analysis of active components of botanicals and their biologic activity. He published more than 25 scientific articles in peer-reviewed journals. Dr. Sarma holds a Pharmacist degree and a Ph.D. in pharmaceutical sciences (pharmacognosy) from Banaras Hindu University, India.

USP Botanical Standards – A Comprehensive Approach for Quality

Botanical quality standards for identity, purity, strength, and composition, with limits on contaminants are critical to ensuring the safety and the purported benefits from the herbal medicine or botanical dietary supplement products. The inherent complexities with botanicals demand use of orthogonal methods that are fit for purpose and can discriminate closely related species. This presentation will describe the *United States Pharmacopeia* collaboration with global stakeholders and expert volunteers in the development of transparent public quality standards (monographs, general chapters and Reference Standards) for herbal medicines and botanical dietary supplements that are published in the USP *Dietary Supplements Compendium* (<http://www.usp.org/dietary-supplements/overview>) and the *Herbal Medicine Compendium* (<http://hmc.usp.org/>). In order to define all attributes of quality, USP monograph contains the specification for the article, which includes tests, procedures, and acceptance criteria. In addition, USP's monographs include several components, including definition, description, packaging, storage, and labeling statements. The voluntary, independent, third-party verification and GMP audit services offered by USP for dietary supplement finished products and dietary ingredients helps ensure that what's on the label is in the bottle in the right purity and strength and that manufacturers have good quality systems and may also help mitigate regulatory risks by preparing manufacturers for GMP inspection. Considering the international commerce of botanicals across traditional systems, global public standards and the verification program can help manufacturers in meeting regulatory requirements through science-based specifications, and can facilitate label uniformity and international trade of quality herbal medicine and dietary supplements.

Ruchi Singh, Ph.D.

Department of Medicinal Plant Science
Dev Sanskriti Vishwavidyalaya,
Gayatrikunj-Shantikunj, Haridwar (Uttarakhand)
INDIA



Dr. Singh is an Assistant Professor in Department of Medicinal Plants' Sciences, School of Biological Sciences at the Dev Sanskriti University where she has been a faculty member since 2016. She is also working as Head-in charge of the Quality Control of herbal drug, Chemistry Division at Shantikunj Pharmacy since 2007. Her research interests lie in the area of extraction, isolation, identification and applications of phytochemicals as well as the ethno medicinal uses of herbal drugs and their fumes. She has collaborated actively with researchers in several other disciplines of Biological Science. She has participated in many national and international conferences. For her scientific contributions she has received Young Scientist Award from Uttarakhand Council of Science & Technology.

Innovative Research on Herbal Inhalation Therapy

We have carried out long-term research on Indian herbal/plant medicines with scientific evaluation and validation. The major/distinct projects completed till date in collaboration with scientists of global repute include — phytochemical analysis of several Himalayan herbs, assessment of therapeutic effects of fresh herbal decoction against to commonly used dry herbal powders, identification of expiry date of dry herbal preparation, neutron activation analysis of micronutrients of a unique herbal brain tonic (*Pragya Peya*) prepared in our laboratory, study of distinguished health-benefits (e.g. synergistic effects) of Ayurvedic herbal medicinal preparation as compared to the synthetic phytochemical drugs, analysis of antimicrobial and antioxidant activity of certain aromatic essential oil containing natural products, etc.

Scientific research on herbal inhalation therapy (*Yagya-Therapy*, *Yagyopathy*) is our most recent and distinct contribution. In this ethno-Indian mode of herbal treatment, medicinal vapors, gases, phytochemicals, etc, released through controlled processing of specific herbal/plant medicinal preparations in the fire of *Yagya* (fire-ritual in specifically designed fire-pit), are inhaled by the participants (patients). Our research on multiple aspects of *yagya-therapy* has shown it as a trend-setting and very effective mode of pulmonary drug administration. Most importantly, it also offers added benefits of — cost-effectiveness, possibility simultaneous treatment of several patients, holistic health benefits due to synergistic effects healthy nutrients used in *yagya*. Significantly, this mode of herbal/ inhalation therapy is also found promising in environmental purification. Our research projects completed (and published) so far include *in-vitro* experiments, pharmaco-kinetic modeling and analysis, and clinical trials on certain diseases including psychological disorders. Apart from extended studies for wider therapeutic and pollution-control applications, our ongoing and planned projects also incorporate comprehensive pharmaco-chemical analysis of the outputs of the individual herbs and their combinations in the herbal preparation (*havan-samagri*) used in *yagya* for specific healing effects.

Shraddha Thakkar, Ph.D.,
Principle Investigator
Division of Bioinformatics and Biostatistics
US FDA/NCTR
USA



Dr. Thakkar works at FDA's National Center for Toxicological Research. Her research interests are in applying bioinformatics and cheminformatics for study of toxicity and drug development with specific interest in drug-induced liver injury. She has received multiple research and leadership awards regionally and nationally and within FDA. That includes Genentech Innovation in Biotechnology Award from American Association of Pharmaceutical Scientist (AAPS), Margret C. Etter Student lecturer award from American Crystallography Association, and Outstanding Service award from FDA. In addition to her work in predictive toxicology, Dr. Thakkar holds 14 international patent and multiple publications in area of drug development for radiation protection, leukemia and atherosclerosis. Her current area of research includes development of methods and classification to enhance the understanding and prediction of drug-induced liver injury. Dr. Thakkar has adjunct appointments at both University of Arkansas for Medical Sciences and University Arkansas at Little Rock (Assistant Professor). Furthermore, Dr. Thakkar was elected as Board member of the Mid-South Computational Biology and Bioinformatics Society (MCBIOS) in 2014 and served as President for the Society from 2016-2017. She is also served as the Chair of Pharmacogenomics Group at AAPS and Personalized Medicine community at AAPS.

Developing Safer Botanical Medicine Using Chemoinformatics Approaches

There is an unmet need for radioprotectors, compounds that protect against radiation injury in the event of radiation accidents or terrorism scenarios. In this context, Vitamin E is a very well-known anti-oxidant that scavenges the free radicals produced by radiation exposure. Vitamin E family includes eight different isoforms including four tocopherols (α , β , γ and δ) and four tocotrienols (α , β , γ and δ), which are collectively known as tocols. The standard vitamin E containing preparation sold in the market is α - tocopherol. The main reason for this is that AT has the slowest rate of elimination ($t_{1/2}$ = 18 h) and thus it can be used for once-a-day administration. However, the therapeutic efficacy of AT evaluated on multiple indications has been disappointing and rather poor. On the other hand, there is a rapidly increasing number of studies that show that the tocotrienols have a much superior biological activity compared to the tocopherols for many indications, including radioprotection. Using in silico techniques, a team of researchers at UAMS were able to design a new kind of vitamin E analogues, named the tocoflexols, which have the both the superior bioavailability of the tocopherols and the superior bioactivity of the tocotrienols.

Franz Ulberth, Ph.D.

Head of the Fraud Detection and Prevention Unit at the European Commission's Joint Research Centre (JRC)
Ispra, ITALY



Franz Ulberth is Head of the Fraud Detection and Prevention Unit at the European Commission's Joint Research Centre. Franz graduated (PhD) in "Food Science and Biotechnology" from the University of Natural Resources and Applied Life Sciences (BOKU) in Vienna, Austria. In 1994 he was appointed professor of food chemistry at the same university. Franz joined JRC in 2002 as a programme co-ordinator for food and environmental reference materials. In 2007 Franz was nominated Head of the Food Safety and Quality Unit. As of July 2016 he heads a newly created Unit devoted to detection of fraud in the food chain and selected consumer goods such as tobacco. He represents the Joint Research Centre in relevant food related technical committees of standards developing organisations such as the European Committee for Standardization, International Organization for Standardization, AOAC International and the Codex Alimentarius. Franz served for a long time on the editorial board of *Food Chemistry*, *European Journal of Lipid Science and Technology*, and currently is editorial board member of *Food Additives and Contaminants*.

Fraud in Dietary Supplements and Foods

International collaboration on the safety of food ingredients and supplements is already well established, while for authenticity this is not yet the case. There is a great need for international harmonisation in order to be able to detect and, what is more important, prevent or at least minimise fraud in the food chain. Therefore, the fight against fraudulent manipulations of ingredients for food products as well as food supplements calls for a global approach involving cooperation and consultation among all stakeholders at all levels of the food chain. Prevention of fraud in the agri-food chain and promotion of authentic products is a major element to assure the commercial success of high-value agri-food products on international markets. Losing reputation in this area will negatively impact on competitiveness and profitability of honest farmers and business operators. On top, the basic right of consumers to have access to authentic products has to be protected.

The Joint Research Centre of the European Commission has long-standing expertise in food science including authenticity research and expertise in developing, applying and validating analytical methods to detect fraud in the food chain. The presentation will review initiatives of the European Commission to fight fraud in the food chain and address needs and research gaps that can only be plugged by international cooperation.

Nurisha Wade

Senior Director, Strategic Marketing and Program Operations
United States Pharmacopeia (USP)
Rockville, MD, 20852
USA



Nurisha Wade is the Sr. Director for Strategic Marketing and Program Operations for USP. She has over 18 years' experience in the food and dietary supplement industry with a specific focus on promoting consumer health and wellness. Prior to joining USP, Mrs. Wade held various roles in for McCormick Spice Co., Campbell Soup Company and Morton Salt Company. She has a Bachelor of Science in Chemical Engineering from Howard University and a Masters in Business Administration from University of Maryland Smith School of Business.

USP Botanical Standards – A Comprehensive Approach for Quality

Botanical quality standards for identity, purity, strength, and composition, with limits on contaminants are critical to ensuring the safety and the purported benefits from the herbal medicine or botanical dietary supplement products. The inherent complexities with botanicals demand use of orthogonal methods that are fit for purpose and can discriminate closely related species. This presentation will describe the *United States Pharmacopeia* collaboration with global stakeholders and expert volunteers in the development of transparent public quality standards (monographs, general chapters and Reference Standards) for herbal medicines and botanical dietary supplements that are published in the *USP Dietary Supplements Compendium* (<http://www.usp.org/dietary-supplements/overview>) and the *Herbal Medicine Compendium* (<http://hmc.usp.org/>). In order to define all attributes of quality, USP monograph contains the specification for the article, which includes tests, procedures, and acceptance criteria. In addition, USP's monographs include several components, including definition, description, packaging, storage, and labeling statements. The voluntary, independent, third-party verification and GMP audit services offered by USP for dietary supplement finished products and dietary ingredients helps ensure that what's on the label is in the bottle in the right purity and strength and that manufacturers have good quality systems and may also help mitigate regulatory risks by preparing manufacturers for GMP inspection. Considering the international commerce of botanicals across traditional systems, global public standards and the verification program can help manufacturers in meeting regulatory requirements through science-based specifications, and can facilitate label uniformity and international trade of quality herbal medicine and dietary supplements.

Z. Alex Xu, M.D., Ph.D

Chief Scientist (Pharmacology and Toxicology)
Center for Drug Evaluation
China Food and Drug Administration
Beijing, CHINA



Dr. Xu is currently working in Center of Drug Evaluation (CDE), Chinese Food and Drug Administration (CFDA), as chief scientist in pharmacology and toxicology. He worked as a senior Pharmacologist/Toxicologist and have reviewed applications of drug and biologic products for various therapeutic areas in the Office of New Drugs (OND) at US Food and Drug Administration, Center for Drug Evaluation and Research (US FDA/CDER). Prior to joining FDA, he worked as a senior scientist in pharma/toxicogenomics in Gene Logic Ltd. Dr. Xu received a Master degree in pathology and PhD degree in pharmacology and toxicology from the University of Arkansas for Medical Sciences. He had his postdoctoral training in the National Center for Toxicological Research (NCTR). Dr. Xu has over 20 year experience in Toxicology and is a Diplomate of American Board of Toxicology (DABT) since 2005. He is a full member of Society of Toxicology (SOT) and the president of the American Association of Chinese in Toxicology (AACT).

Improving the Drug Review System to Accelerate New Drug Development in China

The effort to improve the drug regulation system by the Chinese government has never ceased during the last decades. However, changes have never been so dramatic until the last couple years. During the past couple years, China FDA (CFDA) strived on establishing a drug review system that could be comparable with the international standard. New policies and guidance were published one after another. In 2017, CFDA joined ICH as a regulatory member. This significantly accelerated the process of CFDA reform. As part of the reform, CFDA made great efforts to improve the drug review systems so that new drugs may enter the market quickly after thorough investigation. The goal of this reform is to establish a drug review system that may be in line with the international standards. During the past 2 years, great steps were taken on the adoption and implementation of guidance released by international organizations, establishment of review teams based on clinical indications, application of advanced review concepts and theories, improvement of established communication system with the Sponsors, modifications on the priority review criteria, and shortening review time, etc. This presentation will briefly introduce the reform measures that have been taken, discuss the current status and the impact on new drug development with a focus primarily on botanical drug products.

William Yan, Ph.D.

Director of the Bureau of Nutritional Sciences, Food Directorate
Health Canada
Ottawa, Ontario
CANADA



Dr. William Yan obtained his Master degree in Microbiology and Ph.D. degree in Medical Microbiology and Infectious Diseases from the University of Alberta. He completed his post-doctoral training at Tufts University Medical School in Boston, MA before beginning his career in Health Canada as a Research Scientist in 1995. Between 1999 and 2009, he was Head of the Office of Biotechnology in the Food Directorate, Chief of the Evaluation Division in the Bureau of Microbial Hazards, and Director of the Health Effects Division of the Pest Management Regulatory Agency. In 2010, Dr. Yan was appointed as Director of the Bureau of Nutritional Sciences in the Food Directorate. Since then, he has provided leadership in the Bureau's work on developing nutritional standards and regulations as well as pre-market assessment of novel foods, novel fibres, health claims and infant formulas. He is currently leading the work on Supplemented Foods as well as projects under Health Canada's Healthy Eating Strategy such as sodium reduction and nutrition labelling initiatives.

Regulation and Safety Assessment of Supplemented Foods – A Canadian Perspective

Supplemented foods are broadly defined by Health Canada as pre-packaged products that are manufactured, sold or represented as foods, which contain added vitamins, minerals, amino acids, herbal and/or bioactive ingredients. These ingredients may perform a physiological role beyond the provision of nutritive requirements. Supplemented foods not compliant with the Canadian Food and Drug Regulations can be the subject of an application to Health Canada for Temporary Marketing Authorization. Approval allows temporary sale of products assessed as unlikely to pose a risk to health while gathering data from the applicant to inform development of evidence-based regulations. The goal is to facilitate market access for safe supplemented foods under the same post-market regulatory approach that applies to most other categories of foods. The current status of regulatory development for supplemented foods, as well as some of the associated challenges and evidence gaps, including types of foods appropriate for supplementation, risks associated with chronic exposure when consumed ad libitum, replacement or addition to supplement use, and labelling needed to help consumers make an informed choice, will be addressed.

Poster Presentations

Poster Number: 1

Presenter name: Weida Tong Ph.D.

Title: Comprehensive Assessment of Hepatotoxicity Induced by Herbal and Dietary Supplements

Authors: Dianke Yu¹, Minjun Chen¹, Sanlong Wang⁴, Suzanne Fitzpatrick², Sau (Larry) Lee³, Rajiv Agarwal³, Jinhui Dou³, Baitang Ning¹ and Weida Tong^{1*}

Affiliations: ^{1*}Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, Jefferson, Arkansas 72079 ²Center for Food Safety and Applied Nutrition, College Park, Maryland, 20740 ³Center for Drug Evaluation and Research, Silver Spring, Maryland, 20993 ⁴NIFDC, China

Comprehensive Assessment of Hepatotoxicity Induced by Herbal and Dietary Supplements

Cases of herbal and dietary supplements (HDS) associated liver injury (i.e., HDS-induced liver injury) in clinics have been widely reported. However, HDS are generally not studied and approved as drugs and their regulation is less strict in many countries. The rise in use of HDS in the U.S. market increases the risk of liver injury in certain populations. Specifically, the use of HDS is more popular in women and minority population that consequently leads a higher risk of hepatotoxicity in these groups.

In this study, we conducted a comprehensive assessment of hepatotoxicity of HDS to better understand its impact on public health, especially for women health. First, unique Latin and common names of 42 HDS popularly used in the U.S. market were identified based on the European, U.S. or Chinese pharmacopoeia; and then information related to these HDS including their application, hepatotoxicity, mechanisms, HDS-drug interaction and sex differences, was collected from monographs, web databases and literature data, using the Latin names of HDS as keywords. We found that 26 HDS (62.0%) were associated with liver injuries, and the clinical patterns of hepatotoxicity vary. Besides, 20 HDS (47.6%), such as Black Cohosh and kava kava, are potentially interacted with other drugs. Importantly, 17 HDS (40.4%) more frequently exhibited hepatotoxicity in women than in men. In summary, the HDS hepatotoxicity dataset collected from diverse sources provides a single entry point for better studying HDS-induced liver injury, which should benefit public health, especially women's health. *This study was supported by Food and Drug Administration Office of Women's Health (OWH).*

Poster Number: 2

Presenter name: Jay Gandy, Ph.D.

Title: An Online Graduate Certificate in Regulatory Sciences Developed in Partnership Between the University of Arkansas for Medical Sciences (UAMS) and NCTR

Authors: Jay Gandy, Ph.D.

Affiliations: University of Arkansas for Medical Sciences

An Online Graduate Certificate in Regulatory Sciences Developed in Partnership Between the University of Arkansas for Medical Sciences (UAMS) and NCTR

Jay Gandy, Ph.D., Regulatory Sciences Program, Department of Environmental & Occupational Health, University of Arkansas for Medical Sciences, Little Rock, AR, USA

UAMS initiated an innovative Regulatory Sciences Training Program in 2012 under a Memorandum of Understanding between UAMS, the U.S. FDA and the State of Arkansas. The program is built on long-standing interactions between UAMS and the U.S. FDA's National Center for Toxicological Research (NCTR), located just 30 miles south of the UAMS campus. The curriculum for a Graduate Certificate in Regulatory Science was developed jointly between UAMS faculty and FDA scientists who, along with scientists from the private sector, teach the courses in the program.

The goals of the program are to 1) provide students with insight into the complexities of the laws, regulations, policies, risk assessments, risk-benefit analyses and risk management processes associated with drug and medical device development and food safety; 2) foster leadership in regulatory science of industry, government and academia; and 3) provided students a more competitive background for regulatory science-based careers. Initial student enrollment was double preliminary projections for the program, and has remained steady, with 60 graduates to date.

The curriculum consists of 4 courses: Food and Drug Regulations, Methods in Product Safety Assessment/Risk Assessment, Clinical Trials Design and Management and Good Regulatory Practices (GLPS, GCPs, GMPs). All the required courses for the Graduate Certificate in Regulatory Sciences are now fully online asynchronous classes. What began as a program targeted towards local students is now accessible to individuals globally. The online curriculum allows students from around the world to complete the Graduate Certificate on their own schedule.

For additional information visit: <http://publichealth.uams.edu/regulatory-sciences/>

Poster Number: 3

Presenter name: Qi Liang Ph.D.

Title: A Rapid Screening Method for Sibutramine Hydrochloride in Natural Herbal Medicines and Dietary Supplements

Authors: Honghao Wang[†], Rui Feng, [‡] Ruisi He, and Qi Liang^{†, *}

Affiliations: [†]Guangdong Provincial Institute for Drug Control, Guangzhou 510180, China, [‡]Research Center of Chinese Herbal Resource Science and Engineering, Guangzhou University of Chinese Medicine, Guangzhou 510006, China,

[§]School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006, China

A Rapid Screening Method for Sibutramine Hydrochloride in Natural Herbal Medicines and Dietary Supplements

Herbal weight loss supplements *which* contain adulterants such as sibutramine hydrochloride can result in serious adverse health events including death. In this work, a colorimetric precipitation-based rapid screening method for illegal adulteration of sibutramine hydrochloride in natural herbal medicines (NHM) and dietary supplements (DS) is established. While a variety of chromatography- and electrophoresis-based *methods* have been reported for identifying this analyte from food samples, adoption of these techniques have been limited due to their high costs, complicated sample preparation procedures, and costly analytical infrastructure. In the present work, we report a simple handheld kit for sibutramine. The performance metrics of this method identifying include an average detection time of approximately 3 minutes, which is markedly shorter than conventional methods (HPLC or HPLC-MS, etc.) The detection limit is 0.13 mg per aliquot, the accumulated accuracy is 99.02% (n = 820), the sensitivity is 100% (n = 278), and the accumulated specificity is 98.52% (n = 542). The rapid test kit developed from this screening method was evaluated by the Division of Pharmaceutical Analysis of the US Food and Drugs Administration. In *conclusion*, this method is a rapid, simple, and low-cost tool for the detection of sibutramine in NHM and DS with superior selectivity and sensitivity. This approach is especially suitable for under-developed settings because it can be employed onsite without any instrumentation. This approach could also be used as a pre-screening method before further instrumental analysis.

Poster Number: 4

Presenter name: Jin Hongtao Ph.D.

Title: Acute Toxicity Screening of Different Extractions, Components and Constituents of Polygonum Multiflorum Thunb. on Zebrafish (*Danio rerio*) Embryos in vivo

Authors: Jian-Bo Yang^{a1}, Wan-Fang Li^{b1}, Yue Liu^a, Qi Wang^a, Xian-Long Cheng^a, Feng Wei^a, Ai-Guo Wang^b, Hong-Tao Jin^{b*}, Shuang-Cheng, Ma^{a*}

Affiliations: ^aResearch and Inspection Center of Traditional Chinese Medicine and Ethnomedicine, National Institutes for Food and Drug Control, State Food and Drug Administration, Beijing 100050, China, ^bState Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China

Acute Toxicity Screening of Different Extractions, Components and Constituents of Polygonum Multiflorum Thunb. on Zebrafish (*Danio rerio*) Embryos in vivo

Polygonum multiflorum Thunb. has been used widely in East Asia in treatment of diseases associated with aging. However, there are many reports referred to the toxicity of *P. multiflorum*, especially for liver adverse reactions. The toxicity of it is caused by over dosage or by the herb itself remains unclear. The aim of this study was to study the toxicity of different extractions, components and constituents of *P. multiflorum*, which were assessed in zebrafish embryos. Firstly, the difference of extracting solvent to the toxicity of *P. multiflorum* was researched to probe the influence of usages to the safety of *P. multiflorum*. The toxicity of 70% EtOH extract is considerably higher than that of other extracts. Secondly, 70% EtOH extract was subjected to macroporous resin (DM-8) eluting with a gradient of water and EtOH (H₂O, 25% EtOH, 40% EtOH and 95% EtOH) to give four components (A–D). The toxicity of the component (D) showed higher than the other components (A–C). Thus, the component (D) was taken more attentions to research. Lastly, study on the chemical constituents of the component (D), 27 compounds, including 7 anthraquinones (1–7), 8 stilbenes (8–15), 7 anthrones (16–22), 3 cinnamic acid amides (23–25), 2 naphthols (26–27) were isolated and assessed in zebrafish embryos. Compounds 1–3, 16–22 and 26–27 showed severe toxicity against the zebrafish embryos while other compounds, such as stilbenes, showed no obvious toxicity.

* Corresponding authors.

¹ These authors contributed equally to this work.

E-mail addresses: Jinhongtao@imm.ac.cn (H.-T. Jin), masc@nifdc.org.cn (S.-C. Ma).

This project was financially supported by the National Natural Science Foundation of China (Nos. 81773874 and 81703665), the CAMS Initiative for Innovative Medicine (CAMS-I2M-1- 010) and Youth Research Fund of Peking Union Medical College in 2017 (2017350004).

Poster Number: 5

Presenter name: Hiroki Nakae_Ph.D.

Title: Council for Industrial Use of Biological and Environmental Repositories (CIBER): Japanese Activity for Biobanking Sustaining Reproducibility

Authors: Hiroki Nakae^{1,2}, Junko Ikeda^{1,2}, Koh Furuta^{2,3}

Affiliations: ¹Japan Bio Measurement and Analysis Consortium (JMAC), Tokyo, Japan, ²Council for Industrial Use of Biological and Environmental Repositories (CIBER), Tokyo, Japan, ³Kanagawa Cancer Center, Yokohama, Kanagawa, Japan

Council for Industrial Use of Biological and Environmental Repositories (CIBER): Japanese Activity for Biobanking Sustaining Reproducibility

Reproducibility is in crisis. Recently, scientific papers in the biomedical field have been reported not to be reproducible in a substantial rate (Begley C. G. and Ellis L. M, Nature 483, 531–533 (2012)). Difficulties in collection of samples in certain range of quality for human subject research is not only researcher's problem but also the social problem. Researchers cannot reach a reliable outcome without understanding human diversity by collecting samples from various regions covering major variations in the target analyte fitting for research purpose. Furthermore, those samples should be collected and stored in a certain condition by global consensus. This situation is leading to the ground swell of recognition that biobanking is indispensable for realizing reproducible scientific research in bio-medical field including pharma-industry.

Based on such background, CIBER (Council for Industrial use of Biological and Environmental Repositories) has been brought into creation in Japan, as a counterpart of ISBER (International Society for Biological and Environmental Repositories), coordinated by JMAC (Japan bio Measurement & Analysis Consortium).

CIBER intends to play a role of networking of biobanks and standardization. The goal of networking is to encourage Japanese biobanks to join a global network. For this purpose, CIBER is collaborating with ISBER and building a relationship with BBMRI-ERIC to make our samples and associated data registered in their global biobank network. In addition, CIBER is intensively taking part in the standardization of biobanking quality by supporting the development of ISO standard, namely ISO 20387 "Biotechnology -- Biobanking -- General requirements for biobanking". CIBER has also contributed to publish a Japanese version of "ISBER Best Practices (Ver.4)".

CIBER continues the collaboration with JMAC and certification body in biotechnology, named JBCO (Japan Biotechnology Certification Organization). Through the collaboration with the related organizations, CIBER is going on to establish a social infrastructure for bio-industries.

Poster Number: 6

Presenter name: Shraddha Thakkar Ph.D.

Title: Computer-Aided Design and Development of Novel Vitamin E Analogues as Radiation Protectors

Authors: Ujwani Nukala^{1,3}, Awantika Singh^{1,3}, Rajeshkumar Manian⁴, Nukhet Aykin-Burns¹, Darin E. Jones⁵, Mahmoud Kiaei², Philip J. Breen¹, Cesar M. Compadre¹, and Shraddha Thakkar⁴

Affiliations: ¹Department of Pharmaceutical Sciences, ²Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, AR, ³Joint Bioinformatics Graduate Program, University of Arkansas at Little Rock and University of Arkansas for Medical Sciences, Little Rock, AR, ⁴Tocol Pharmaceuticals, LLC, Little Rock, AR, and ⁵Department of Chemistry, University of Arkansas at Little Rock, AR, and ⁶National Center for Toxicological Research/US Food and Drug Administration, Jefferson, AR

Computer-Aided Design and Development of Novel Vitamin E Analogues as Radiation Protectors

There is an unmet need for safe and effective agents that can be used in accidental or terroristic radiological emergencies, as well as to improve the quality of life of patients undergoing radiotherapy. In this context, some of the vitamin E components have shown strong radiation protection effects. Vitamin E family includes eight isoforms, four tocopherols (α , β , γ and δ) and four tocotrienols (α , β , γ and δ) (Figure 1A), with the tocotrienols being more active, but the tocopherols have better bioavailability. Tocotrienol's shorter circulation half-life is due to their low affinity for α -tocopherol transfer protein (ATTP), the liver protein that maintains the tocol's plasma levels by recycling them into the systemic circulation (Figure 1B). Intrigued by the fact that the tocols show dramatic differences in their pharmacokinetic and pharmacological profile, despite relatively minor structural differences, we have conducted computational and experimental analysis of their structure and properties. The results of our analysis suggests a paradigm in which the observed differences can be explained by a multifactorial function:

"Tocol therapeutic efficacy = F_n (intrinsic activity, elimination rate, cell-uptake)"

We have used this paradigm to develop novel vitamin E analogues that show rapid cell-uptake and enhanced bioavailability while maintaining the strong radioprotective activity of the tocotrienols.

Poster Number: 7

Presenter name: Jun-young Yang Ph.D.

Title: Introduction of Korea National Toxicology Program – Toxicity Studies on Herbal Medicines

Authors: Jun-young Yang, Jong Kwon Lee, Sooyeul Cho, Hyun-Kyung Kim, Ji Hyun Seok, Jin hee Lee and Jayoung Jeong

Affiliations: Toxicological Evaluation and Research Department, National Institute of Food and Drug Safety Evaluation (NIFDS), Ministry of Food and Drug Safety (MFDS), Cheongju, Republic of Korea

Introduction of Korea National Toxicology Program – Toxicity Studies on Herbal Medicines

Korea National Toxicology Program (KNTP) is a major project of NIFDS, which consists of toxicity studies on the substances lacking toxicological information and thus aims to support safety management of food and medicine. KNTP has been running since 2002 and mainly focused on toxicity tests on herbal medicines. Herbal medicines have been taken for thousands of years based on users' experience, and there is a lack of toxicological data to ensure safety. Through KNTP, 59 medicinal herbs were tested mainly for single dose toxicity, 90 days repeated dose toxicity and genotoxicity so far. Usually herb was extracted with hot water for 4-6 hours, and the extract was dried and provided for toxicity tests. The histopathological results of each toxicity test were peer-reviewed by independent pathologists. Full results of toxicity study were reviewed by the Scientific Advisory Committee of NIFDS and put together into a KNTP toxicity report (TR). Moreover, the results of KNTP studies were reflected on regulatory policies on food and drug safety, Korea MFDS. *Cynanchum wilfordii* Hemsley is a medicinal herb, which has been used as an ingredient of oriental medicines in Korea for a long time. Recently consumption of this herb increased rapidly as an ingredient of food and dietary supplements, thus safety concerns arose. 90 days repeated toxicity studies were performed with hot water extract as well as crushed powder of *Cynanchum wilfordii* Hemsley, separately. No toxicity was observed with hot water extract, however, severe weight loss of tested rats occurred with crushed powder of *Cynanchum wilfordii* Hemsley. Based on these findings, Korea MFDS revised the relevant regulations that consumption *Cynanchum wilfordii* Hemsley is restricted to hot water extract, as an ingredient of food or diet supplements. KNTP would continue to expand toxicity studies on herbal medicines and contribute to secure our citizen's health.

Poster Number: 8

Presenter name: Wang Yuxin Ph.D.

Title: A Hepatoprotection Study of Radix Bupleuri on Acetaminophen-Induced Acute Liver Injury

Authors: Wang Yuxin^{a,b}, Du Yi^a, Liu Xiafei^a, Lu Yihong^{a,*}, Meng Changhong^a, Shi Qingshui^a, Wang Guangji^b

Affiliations: ^a Jiangsu Institute for Food and Drug Control, No.17 Kangwen Road, Nanjing 210019, Jiangsu, China, ^bKey Lab of Drug Metabolism and Pharmacokinetics, China Pharmaceutical University, No.24, Tongjiaxiang Street, Jianye District, Nanjing 210009, Jiangsu, China

A Hepatoprotection Study of Radix Bupleuri on Acetaminophen-Induced Acute Liver Injury

* Corresponding author. E-mail addresses: yihonglu@163.com)

Radix Bupleuri (RB), a well-known traditional Chinese medicine (TCM), has been widely used for the treatments of influenza, fever, inflammation, malaria, menstrual disorders, and hepatitis in China for over 2000 years. Modern pharmacology research also proved that RB had hepatoprotective effects. As a common analgesic drug, acetaminophen (APAP) can cause acute oxidative stress and liver injury. Considering the combination use of acetaminophen (APAP) and preparations containing RB in clinic, drug-drug interaction is great concern to us. To investigate the hepatic effect of RB, an animal model of acute liver injury (ALI) was induced by APAP after pretreated with the aqueous extraction of RB for three consecutive days. Compared with APAP model group, biochemical and histological results showed lower serum AST and ALT levels as well as less liver damages when pretreated with RB. Pharmacokinetic study of toxicity marker acetaminophen-cysteine (APC) revealed a lower exposure level in rats, suggesting RB alleviated APAP-induced liver damage by preventing GSH depletion. The results of cocktail approach showed a significant activity inhibition of CYP2E1 and CYP3A1. In further investigation, the protein expression of CYP2E1 and CYP3A1 were inhibited significantly, while no obvious effect on gene expression was found in pretreated group. Therefore, these results clearly demonstrate that pretreatment of RB exhibited significant protective action toward APAP-induced ALI, and the mechanism of protection partly through the inhibition of CYP450 activity which probably occurred in the translation process instead of the transcription of genes.

Poster Number: 9

Presenter name: Zhuhong Zhang Ph.D.

Title: Mechanistic Study of *Ginkgo Biloba* Leaf Extract-Induced DNA Damage in Human Hepatic Cells

Authors: Zhuhong Zhang^{1,2}, Lei Guo³, Nan Mei^{2*}

Affiliations: ¹School of Pharmacy, Key Laboratory of Molecular Pharmacology and Drug Evaluation (Yantai University), Ministry of Education, Collaborative Innovation Center of Advanced Drug Delivery System and Biotech Drugs in Universities of Shandong, Yantai University, Yantai, 264005, China

²Division of Genetic and Molecular Toxicology, ³Division of Biochemical Toxicology, National Center for Toxicological Research, Jefferson, AR 72079, USA

Mechanistic Study of *Ginkgo Biloba* Leaf Extract-Induced DNA Damage in Human Hepatic Cells

Ginkgo biloba extract has been used as dietary supplement for a wide range of remedies. *Ginkgo biloba* extract consists of various constituents including flavonol glycosides and terpene lactones. *Ginkgo biloba* extract has been shown to increase an incidence in liver tumors in mice in a standard 2-year bioassay evaluated by the National Toxicology Program. In this study, the DNA damaging effects of *Ginkgo biloba* extract and many of its constituents were evaluated in HepG2 cells and the underlying mechanism was determined. A molecular docking study revealed that quercetin showed a higher potential to interact with topoisomerase II (Topo II) than did the other *Ginkgo biloba* constituents, and this *in silico* predication has been confirmed by using a biochemical assay to study Topo II enzyme inhibition. Moreover, as measured by the Comet assay and the induction of gamma-H2A.X, quercetin, followed by keampferol, appeared to be the most potent DNA damage inducer in HepG2 cells. In Topo II knockdown cells, DNA damage triggered by quercetin was dramatically decreased, indicating that DNA damage is directly associated with Topo II. In addition, the Topo II inhibitory effect and DNA damage were also observed when cells were treated with commercially available *Ginkgo biloba* extracts. Our findings suggest that quercetin- and *Ginkgo biloba*-induced genotoxicity and tumorigenicity may be the result of Topo II inhibition.

Poster Number: 10

Presenter name: William Slikker, Jr., Ph.D.

Title: Global Coalition for Regulatory Science Research (GCRSR) - The Past, Present and Future

Authors: William Slikker, Jr., Shraddha Thakkar and Weida Tong, Ph.D.

Affiliations: National Center for Toxicological Research, US Food and Drug Administration, Jefferson, Arkansas, USA

Global Coalition for Regulatory Science Research (GCRSR) - The Past, Present and Future

The Global Coalition for Regulatory Science Research (GCRSR) was established in 2013 under the leadership of the US-FDA. The mission of GCRSR is to foster the uptake of emerging technologies by engaging regulatory agencies in the global context. This is an international coalition with the objectives of facilitating education, scientific training and scientific exchanges in the field of regulatory science. It focuses on research to support regulatory decision making by identifying and promoting best practices to understand and interpret data from innovative technologies such as genomics. To date, GCRSR discussions have been focused on (1) defining the role of global research collaborations in advancing regulatory science and its impact on public health, (2) exploring the future of regulatory science research as a tool for advancing regulatory science in the areas of food safety and medical products, and (3) developing strategies for training of regulatory scientists in a global setting. Consequently, its main activities involve (1) holding workshops and scientific meetings, including the annual Global Summit on Regulatory Science, to discuss the current development of new technologies and their potential utility in the regulatory settings; (2) exchanging scholars and students for the purpose of providing education and training courses; and (3) enhancing the development and use of regulatory science principles. To achieve these goals, the annual GSRS meetings have been instituted. GSRS conferences provide a venue where regulators and researchers can meet and develop collaborations to address the challenges and needs in the interest of advancing regulatory science. Seven meetings have been conducted so far, with the first (GSRS2011) taking place in the US (Slikker et al., 2012), GSRS2012 in China (Miller, et al., 2013), GSRS2013 in the US (Howard, et al.), GSRS2014 in Canada (Tong, et al., 2015), GSRS15 in Italy (Healy et al., 2016), GSRS16 (Patri, et al., 2016) in the US and GSRS17 in Brazil (Slikker et al., 2018).

Poster Number: 11

Presenter name: Narendra G Shah Ph.D.

Title: Efficacy of Micronutrient Fortified Supplementary Foods (Ready to Cook and Ready to Eat) for Children with Moderate Acute Malnutrition (MAM) Using Community Based Approach

Authors: Narendra G Shah (Professor)*† Pushkala Ramchandran (Research Associate, PhD) *, Nikita Patel (Research Assistant) *, Harini Swaminathan (PhD scholar) *, Alka Jadhav (Professor, Paediatrics) **, Priyanka Shinde (Research assistant-nutritionist) **

Affiliations: *Centre for Technology Alternatives for Rural Areas, IIT Bombay, India, **Department of Paediatrics, LTMGH, Sion Mumbai, India

Efficacy of Micronutrient Fortified Supplementary Foods (Ready to Cook and Ready to Eat) for Children with Moderate Acute Malnutrition (MAM) Using Community Based Approach

† Corresponding author (prof.narendra.shah@gmail.com)

Objective: Efficacy of micronutrient fortified supplementary foods of two types ie ready to cook (RTC) and ready to eat (RTE) was evaluated for satisfactory recovery from moderate acute malnutrition (MAM). Children recruited in the clinical trial were provided 1/3rd of their RDA calories and proteins and 75% of micronutrient requirement per day, the remaining coming from their routine daily diet.

Design: A randomized, controlled trial was carried out in the selected *Anganwadis* of Dharavi slums, Mumbai, India. The *Anganwadis* were divided in two groups ie Treatment (T) and Control (C). Children (aged between 6 to 60 months) qualified as MAM based on anthropometry, were further divided into two age groups i.e. Group A- 6 months to 24 months and Group B- 25 months to 60 months. Out of 5667 children screened, 324 were selected for further intervention and monitoring and assigned randomly into T and C *Anganwadis*. Each child in Group A received a ratio of 250-300 kCal and 10-12 g proteins and in Group B 450-500 kCal and 12-15 g proteins, on a daily basis and were fortified with micronutrients (WHO guidelines) using culture-centric foods. The intervention was carried out for 3 months followed by a further 3 months of follow up period. Throughout the 6-month period, the anthropometric data of the children (weight, height and MUAC) was closely monitored on a weekly basis.

Results: Significantly higher weight gain (0.75g/kg/d) was seen in children receiving the supplementary foods compared to the children receiving THR (0.52g/kg/d) at CI of 99 % (p=0.01). Using WHO growth charts (WHZ) we found that 39 % children were brought to normalcy using these fortified foods.

Conclusion: High calorie, high protein, and micronutrient fortified supplementary “culture Centric” foods in combination with nutrition counselling can help in bringing out children from MAM to normalcy using community approach.

Trial registry: ctri.nic.in as [CTRI/2017/08/009260](https://clinicaltrials.gov/ct2/show/study?term=CTRI/2017/08/009260)