IFAPPWORLD
INTERNATIONAL FEDERATION OF ASSOCIATIONS OF PHARMACEUTICAL PHYSICIANS & PHARMACEUTICAL MEDICINE

CONTENT LEAD STORY



## Join the 18th International Conference on Pharmaceutical Medicine

**ICPM 2016 | 18-19 April 2016 | São Paulo, Brazil**

IFAPP and the Brazilian Society of Pharmaceutical Medicine (Sociedade Brasileira de Medicina Farmacêutica – SBMF) warmly invite you to attend ICPM 2016 in April 2016 in São Paulo, Brazil. It is an international forum for pharmaceutical medicine professionals and a unique opportunity for all participants to listen and interact with opinion leaders and main stakeholders from academia, government, pharmaceutical companies, contract research organizations (CROs), and non-governmental organizations (NGOs) in a neutral and friendly environment.

Representatives of the ICPM 2016 Organizing Committee provide answers on relevant questions.

**IFAPP WORLD** • Dr Schmidt, ICPM 2016 and the Brazilian Annual Congress on Pharmaceutical Medicine are organized jointly. What is the challenge in arranging this national and international event?

**Dr Charles Schmidt, SBMF, Brazil** • The primary challenge is to harmonize the interests regarding the conference topics that could attract national and international attendees and then the logistics to reach out with the program to our colleagues all over the world. The scientific committee has had many meetings to appoint the subjects for ICPM 2016 and to ascertain the availability of key >>> >>>

## The Specialist in Medicines Development (SMD) Program – a Pilot in Japan

In promoting pharmaceutical medicine as our organizational vision and mission, the Japanese Association of Pharmaceutical Medicine (JAPhMed) has developed its educational course in collaboration with the Osaka University, which is now recognized as Centre of Excellence (CoE) by PharmaTrain – the first one in Asia. Following this successful development, our next challenge is to introduce the Specialist in Medicines Development (SMD) program as a pilot project in Japan together with Italy and supported by PharmaTrain. Local environment for the implementation of this SMD program is tough, though.

Within the Japanese industry it is traditionally seen as the responsibility of the individual corporations (workplaces) to educate and train their employees and to make them fit for their corporate objectives. Such corporate education and training is mostly limited to departmental operating procedures, and externally certified knowledge, skills and attitudes are less required in their job descriptions. However, the recent worldwide changes in corporate management led to massive outsourcing of business and infrastructures out of many companies As a result, the R&D divisions of pharmaceutical corporations have lost many qualified professionals from their workplaces. [*Please also note the report starting in the center of page 2*].

In academia, where the need of professional education and training in pharmaceutical medicine has largely been ignored, the implementation of the SMD program may not be easy as many of the investigators do not have mentors with the appropriate expertise across the wide range of the medicines development process. Further on, many investigators have little time left for the development of their specialty or lack appreciation to be recognized as specialist in this field. The same is true for other professionals working in clinical research.

The Japanese regulatory authority recently puts more emphasis to foster investigator initiated trials and calls for educational programs (though limited to the clinical development domain), while at the same time they see the training of contract research organization's staff as the responsibility of the sponsoring pharmaceutical company.

In this difficult situation, why and how do we want to introduce the SMD program in Japan?

First, graduates of our CoE courses are interested to further pursue their careers, and they find the internationally recognized specialist title to be important for their future. Recent governmental investments in the Japanese leadership to develop innovative medicines also motivated national organizations in the medicines development field to think and act global. Encouraged by these changes of our environment, we plan to introduce the SMD program in Japan by:

1. Raising awareness of the value of education & training and certification by 3rd parties.
2. Developing a consortium of relevant parties for a wider recognition in the society.
3. Realizing joint recognition of SMDs in industry, academia (and authority).

Although knowledge can be gained by participating in external courses, acquisition of >>>

>>> >>> opinion leaders in the respective fields as speakers and chairs at ICPM 2016. We intend to present a global perspective, which allows the audience to compare various procedures and experiences and gain new insights, which they might implement in their own day-to-day activities. We will prepare a pragmatic, dynamic and exciting program with time enough for fruitful discussions, for networking and also for enjoying the cosmopolitan city of São Paulo.

**IFAPP WORLD** • What will be the main topics of the program and where can interested people find detailed information on that?

**Dr Charles Schmidt** • The main conference topics are related to medical affairs, to pharmacovigilance, to innovation, and regulatory sciences. The detailed program will be available soon at our official website at www.icpm2016.com.

**IFAPP WORLD** • Dr Almeida, when and how should participants register? And what should they organize beside their registration?

**Dr Cesar Almeida, SBMF, Brazil** • Registrations should be performed online at www.icpm2016.com. A special discount on the conference fee is available until the 18th of January 2016. And for members of IFAPP or SBMF we offer a certain reduction of the conference fee.

We recommend that you book your flight early to São Paulo – Guarulhos International Airport. Also >>> competence and professional development require standard definition and consistent supervision in the workplace. This is where the PharmaTrain SMD program is most effective and advantageous to be adopted.

We are now preparing our SMD program jointly together with the national SMD Executive Group (SEG) and the global PharmaTrain Certification Board (gPCB). We also invite a broad range of organizations such as industry associations, national research organizations, academic and professional societies in clinical research, and international site network organizations to join us, hoping that the SMD will soon become the standard for those working in medicines development.

*Dr Kyoko Imamura*
*JAPhMed President, Japan*

please check your health insurance, this is important when traveling internationally. However, although Brazil is a tropical country, you don't need any particular medical prevention when visiting the state of São Paulo. But due to its tropical climate, we recommend to check the whether forecast for São Paulo just before you start your journey – "The Weather Channel" might help you.

Arriving in São Paulo at the international airport you should expect a 30 minutes drive, which takes you to the hotel where ICPM 2016 will be held. For transportation we recommend the official taxis – Guarucoop – located in front of the airport lobby.

**IFAPP WORLD** • São Paulo and Brazil sound fascinatingly exotic for people, who came from other parts of the globe. What can they expect beside the program? And what should they plan?

**Dr Cesar Almeida** • São Paulo is among the world's capitals of sophistication regarding business, culture, entertainment, shopping and gastronomy. It is an obliging city, which stands out for the quality of services offered. It brings together creativity, multiculturalism, elegance, excitement and an infinite number of attractions that please all visitors – museums, cultural centers, parks and green areas, theaters, movie theaters, soccer stadiums, restaurants, bars and night clubs, shopping malls and streets with specialized commerce. Just visit the menu "São Paulo" at www.icpm2016.com for the main sights and attractions of the city and particular web links.

The local currency is the Real. At the international airport in São Paulo and near the hotel there are exchange offices to buy local currency.

IFAPP WORLD • Thank you very much for your detailed answers.

*Interview by Eckhard Böttcher-Bühler, Germany.*

## JAPAN: Benefits from Multi-regional Clinical Trials for New Medicines

# Perspectives on Drug Development in Japan and Asia (Part I)

Asia is a growing market for the pharmaceutical industry, and the involvement of Asian countries from the earlier stages in drug development has become an important strategy for many US-, European-, and Japan-based pharmaceutical companies. This article reviews the drug development situation in the Asian region mostly from Japan's point of view, and looks into the changing paradigm in pharmaceutical R&D in the Asian region.

### Current State of Global Simultaneous Drug Development in Japan

As has been reviewed in the past, Japan started to participate in multi-regional clinical trials (MRCTs) in the late 1990s, and the number of MRCTs has increased since then [1] [2]. Recent survey results among European-based pharmaceutical companies with subsidiaries in Japan are shown in **Figure 1**. Consistent with the past reviews, the number of simultaneous global drug developments as well as the total number of clinical trials has increased after the publication of Basic Principles of Global Clinical Trials in Japan in 2007.

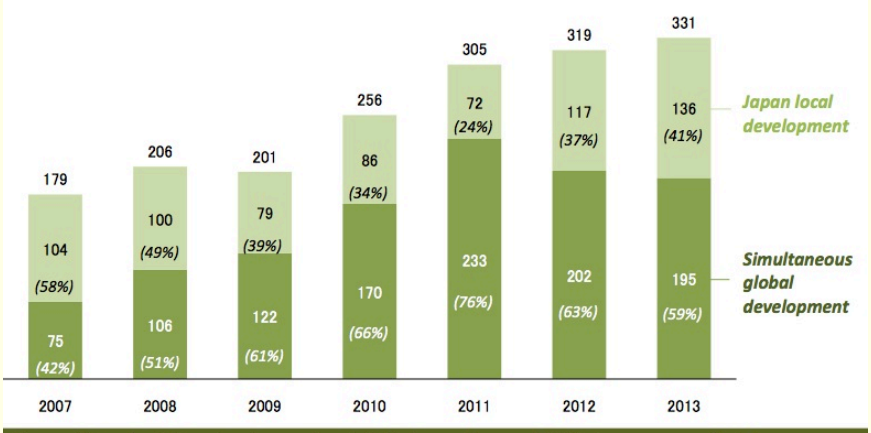


*Figure 1: Trends of drug development projects in Japan [Source: EFPIA Japan survey (data from 15 companies) – printed by permission]*

By the end of March 2014, about 60 pharmaceutical products have been approved by the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) after global simultaneous developments, based on the analysis of results from registered clinical trials. Among these products, >>>

>>> 40 percent of them are drugs in oncologic indications; drugs in the field of diabetes mellitus, cardiovascular and respiratory diseases count more than 10 percent each. Because of the ethnical similarity of the populations in Asian countries, it is a quite popular strategy to go along with multi-national clinical studies involving Asian countries only; these count 25 percent among global studies.

## Benefits from Global Simultaneous Development

There are several benefits regarding global simultaneous development from various points of view. The following paragraphs put a focus on two aspects: (1) the elimination of time lags regarding drug approval in Asia ("drug lag") and (2) the new insight from experiences of MRCTs including ethnic factors.

### Elimination of a "Drug Lag" in Asia

It has been well known that a drug lag has been identified as a critical issue in Japan [2]. The elimination of this drug lag has been a mission of the Japanese government, and this has become a driving force to promote global simultaneous drug development in Japan. The issue of a drug lag was most seriously concerned in the field of oncology, and the need for eliminating the drug lag in this field was urgently desired by patients and physicians. This reflects the fact that the highest numbers of MRCTs and of new drug approvals in Asia could be counted in the therapeutic area of oncology as shown in Table 1.

| Number of MRCTs (total n = 49) [Number of Asian MRCTs] | Therapeutic Area | Ratio |
|---|---|---|
| 19 [3] | Oncology | 39% |
| 7 | Respiratory | 14% |
| 6 [1] | Diabetes mellitus / insulin | 12% |
| 5 [1] | Cardiovascular / thrombosis | 10% |
| 4 [2] | CNS | 8% |
| 3 | Ophthalmology | 6% |
| 2 [2] | Influenza | 4% |
| 2 [2] | Overactive bladder | 4% |
| 1 | Rheumatoid arthritis | 2% |

*Table 1: Multi-regional Clinical Trials (MRCTs) by Therapeutic Area*

The promotion of global simultaneous development has delivered a positive impact on drug development in Japan. Currently, the products approved within a year after the first approval in either US or European countries counts 10, and most of them are again oncology drugs. Further, there have been several products, which obtained the world's first approval in Japan.

Many drugs that have successfully passed a global simultaneous development are currently under regulatory review, and many drugs are currently under development through global simultaneous development. Therefore, it is expected that the drug lag will become a non-issue in Japan in very near future.

### New Scientific Insights

**1. Outcome Data** • Outcome data including the effects on mortality such as overall survival is important to understand the medical value of drugs. To investigate the effects of drug treatments on the outcome endpoints such as mortality, large-scale clinical trials involving multi-regions are usually required. These studies have been commonly conducted in the cardiovascular area and mostly in western countries with high incidence of cardiovascular diseases in the region.

It was very difficult to conduct large-scale clinical trials in a single Asian country from a practical point of view, and therefore, physicians in Asian countries had to rely on outcome data from western countries that may not necessarily be relevant for Asian countries.

Currently, in many drug development programs, large-scale clinical trials investigating outcome end-points are often conducted including Japan and other Asian countries. The data from these trials will provide the additional aspect of the Asian population on the outcome data, and are contributing to better medical care in these regions.

**87 centers in 9 Asian countries** – China, Hong Kong, Indonesia, Japan, Malaysia, Philippines, Singapore, Taiwan, Thailand

Randomization period: ..... March 2006 to October 2007

Randomized patients: ..... 1,217 patients

Approval in Japan: ..... July 2002 – NSCLC: First in the world

Partial Change Approval: ..... November 2011 – NSCLC with EGFRm(+)

NSCLC – Non Small Cell Lung Cancer
EGFRm – Epidermal Growth Factor (EGF) receptor mutation

*Table 2: Iressa Pan Asian Study (IPASS) [according to NEJM 2009; 361:947]*

**2. Ethnic Factors** • On the one hand, the results of clinical trials analyzed with regard to the total population that is statistically and adequately powered are obviously most important in global MRCT for the appropriate interpretation of the outcome. On the other hand, a subgroup analysis by ethnicity also provides unique scientific information about ethnic factors and how they impact the interpretation of the study results.

Commonly identified ethnic factors include genetics, eating habits, and medical care environment including the differences in standard care and the use of concomitant drugs. The analysis of the data based on these factors can provide the information how these factors might have an impact on the drug effects. The information obtained by subgroup analysis could contribute to the improvement in precision in the field of personalized medicine.

In the following paragraphs, the data of several clinical trials are reviewed to consider the impact of ethnic factors on the study results.

**2.1. Iressa Pan Asian Study (IPASS)** • IPASS [3] is an MRCT with over 1,200 patients in 9 Asian countries, which are listed in Table 2. Iressa (gefitinib) was approved in 2002 for the indication of non-small cell lung cancer (NSCLC) without specific subpopulation target. Shortly after its launch, a high incidence of death due to interstitial pneumonitis became the issue.

The trial was conducted to find out the appropriate target population of this drug by investigating the effect of gefitinib versus chemotherapy (carboplatin-paclitaxel) in patients with positive Epidermal Growth Factor (EGF) receptor mutation [EGFRm(+)] and in patients without the mutation [EGFRm(-)]. It was conducted in Asian countries only based on the data indicating a higher incidence of EGFRm(+) in the Asian population as compared to that in the Caucasian population. The effect of Iressa in EGFRm(+) patients was evident:

- In EGFRm(+) patients progression-free survival (PFS) was significantly longer when treated with gefitinib than in those treated with chemotherapy (hazard ratio for progression: 0.48; 95% CI: 0.36 to 0.64; P<0.001).
- In EGFRm(-) patients significantly shorter PFS was observed when treated with gefitinib than in those treated with chemotherapy (hazard ratio: 2.85; 95% CI: 2.05 to 3.98; P<0.001).

These results demonstrated the efficacy >>>

>>> of gefitinib in EGFRm(+) patients with NSCLC.

In addition, a subgroup analysis including Japanese patients only indicated the same trend as compared to the full population results. Based on this data, the indication was revised to be limited to EGFRm(+) in 2011, which contributed to personalized medicine in lung cancer treatment.

It seems obvious that the conclusion from this clinical trial recruiting Asian people is applied to EGFRm(+) patients in the Caucasian population, and therefore, there is no impact of particular ethnic factors on the study results.

However, the higher incidence of EGFRm(+) in the Asian population might have led to the clear demonstration of the efficacy of gefitinib in the EGFRm(+) patients with NSCLC in this Asian study.

*This report, including references, will be continued and finalized in the next IFAPP WORLD issued in December 2015.*

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*This report was first published in "pharmazeutische medizin" 2015, 17/2:106-110 – the journal of the "German Society of Pharmaceutical Medicine".*


25 November 2015
Zurich, Switzerland

# 20th Anniversary: Swiss Annual Symposium in Pharmaceutical Medicine

The 20th Swiss Symposium in Pharmaceutical Medicine (PM) is jointly organized by the Swiss Association of Pharmaceutical Professionals (www.SwAPP.ch) and the Swiss Society of Pharmaceutical Medicine (www.SGPM.ch). SwAPP, founded 1995, is the association for qualified specialists working in the fields of PM and drug development. SGPM was founded 1997 for physicians with or in training for specialization in PM. This has raised questions from IFAPP WORLD, which have been answered by SwAPP and SGPM representatives as follows:

**IFAPP WORLD** • When has the Swiss Medical Council acknowledged the Swiss Medical Specialist title in Pharmaceutical Medicine?

**Dr Annette Mollet, SwAPP Board Member** • The specialist title exists since 1999 in Switzerland and, since its inception, 113 specialist titles have been awarded to Swiss physicians and also to some with other nationalities.

The application for this specialty was acknowledged at first attempt by FMH (Foederatio Medicorum Helveticorum), the Swiss medical association, since colleagues were already working in that field and were acquiring expertise but no official recognition was in place.

**IFAPP WORLD** • Since then, what has changed for physicians working in the fields of PM?

**Dr Martin Traber, SGPM President** • Physicians with the specialization title work in the pharmaceutical industry but there are now also academic colleagues who acquire the title as drug development is not confined to the industry but more and more at institutes, e.g., clinical trial centers at universities. In order to apply for the examination, physicians have to fulfill a very demanding curriculum and, in addition to having gained practice in the clinic, must have worked for certain time periods in various departments of a pharmaceutical company, a contract research organization (CRO), a medicines regulatory body or any other institution accredited by SGPM, e.g., in regulatory affairs, development, drug safety.

**IFAPP WORLD** • How do they cooperate with non-physician experts in PM in day-to-day operations, in particular in the light that they are organized in different societies? What about the jointly organized Swiss Symposium in PM – are there special parts in the program for one or the other PM experts?

**Dr Mirjam Eglin, SwAPP President** • The joint Swiss annual symposium addresses both, the physicians and the non-physicians in their daily challenges for the development of medicines. Physicians working in the pharmaceutical industry cooperate with their non-physician colleagues for example in clinical development by planning and executing clinical trials, dealing with pharmacovigilance and post marketing aspects and the medical-scientific information. Swiss law requires adequate training, but not necessarily a physician's title for tasks in clinical development.

**IFAPP WORLD** • Is the Swiss Medical Specialist title in PM a real great benefit for the matter of PM or is the title just a symbol of prestige?

**Dr Brigitte Franke-Bray, SGPM Board Member** • The title Swiss Medical Specialist in PM is a great benefit for physicians involved in the development of medicines as they are recognized to be experts in this field. The title is equivalent to a title in internal medicine, neurology, gynecology, etc. The training and education towards the title provide the physicians with specific tools for a much better understanding of the complexity of the drug development process.

**IFAPP WORLD** • Thank you for your answers.

*Interview by Eckhard Böttcher-Bühler, Germany.*

## The Flag

IFAPP WORLD is a publication of the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine.

IFAPP, a non-profit organization founded in 1975, acts as an international forum for all pharmaceutical medicine professionals' organizations worldwide by dealing with matters brought to its attention through national member associations.

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