

indenature



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TIME FOR A CHANGE? INDENA IS READY

Valerio Bombardelli (Regulatory Affairs Dept., Indena S.p.A., Milan, Italy)

For almost a century there has been a total predominance of synthetic and pure molecules in western medicine and the regulatory framework has developed accordingly. European regulators are now turning their attention however to herbal medicines and have recognised their traditional role and uses for self-medication purposes. Plants, herbs and their derivatives can now enjoy a simplified pharmaceutical registration in Europe where their safety and efficacy rely on their traditional use, while product quality is assessed through compliance to pharmaceutical GMPs (Good Manufacturing Practices). Indena has carefully monitored the development of these new rules and reviewed them critically. The application, in principle, of the GMPs and the consequent Common Technical Document format can be considered a reasonable approach; the exact reproducibility of the herbal product and its active principle will be ensured, so that their safety may be taken for granted, while their efficacy relies on traditional use. The tasks of the new Committee for herbal medicinal products have raised great interest, as the authority is now competent to develop monographs on traditional herbal medicines along with the well-established use ones. The lack of rules to boost innovation, on the other hand, shows yet again how difficult

it is to bring new plant derivatives into the pharmaceutical market. Good news for innovation hails from the U.S., where the FDA's botanical drug guidance (drafted in August 2000) has been finalised and a team of FDA experts set up to follow botanical drug applications. Under this guidance, clinical trials on botanicals sold as dietary supplements may be conducted, providing the FDA with very limited CMC (Chemistry Manufacturing Controls) and pharmaco-toxicological data (at least for phase 1 and 2 trials). It is widely thought that the FDA will finally regulate the production of dietary supplements by the end of 2004. The new GMPs should cover the whole production chain, which means not only the finished product but also the production of each single dietary ingredient. The proposed rule will govern the design and construction of production sites, quality control procedures, record keeping and much more. In addition, the FDA would also have the authority to determine standards, such as USP compliance, applied by manufacturers throughout production and labelling. Could this be the right time for a serious change in the regulatory and market environment for botanicals in Europe and the United States? Hard to judge, but surely these new regulations demonstrate the need for better substantiated botanical and herbal products with a higher quality profile. Indena will continue to play a crucial role in this new scenario, collaborating closely with stakeholders and authorities. For many years now, the company's natural derivatives have been used as the active principles in clinical trials carried out by NIH and US universities, following precisely those procedures put forward in the Botanical Drug Guidance. Indena heartily welcomes these new regulatory trends too which at last will serve to guarantee the proper quality of plant derivatives. With many herbal extracts in the pipeline which already comply with the new rules and a quality profile formatted in the current CTD style, the Indena emphasis on the highest quality standards may once more be acknowledged.

INDENA OFFICIAL TO JOIN THE FRENCH PHARMACOPOEIA

Dr. Serge Bizot, Quality Assurance Manager at Indena Tours, has been nominated a member of the French National Pharmacopoeia Commission (Commission Nationale de la Pharmacopée) for the year 2004. The Commission's task is to edit the French Pharmacopoeia and complete the National Formulary. This nomination is just the latest to confirm the presence of Indena people within the main international authorities. These include the European Pharmacopoeia, USP (United States Pharmacopoeia), NIH (National Institute

of Health), NCCAM (National Center for Complementary and Alternative Medicine), WHO, Emea, ESCOP (European Scientific Cooperative on Phytotherapy).



DR. EZIO BOMBARDELLI RECEIVES THE VARRO TYLER AWARD FOR RESEARCH IN BOTANICALS

Dr. Ezio Bombardelli, President of the Indena Scientific Board, has received the Varro Tyler Prize for Research on Botanical Dietary Supplements. The occasion was this year's annual conference of the American Society of Pharmacognosy held in Phoenix, Arizona on July 31st.

For the first time in 5 years, the meeting was also sponsored by its European counterpart, the Society for Medicinal Research.

This award, bestowed on one of the world's foremost botanical experts, is testimony to the importance of classical botanical pharmacognosy. Addressing the conference Bombardelli said he was honored to receive the award, which was recognition of his personal commitment and that of Indena to the science of botanicals.

"Pharmacognosy needs to be given special attention to ensure the quality, identity and purity of natural medicines", declared the prizewinner.



Dr. Ezio Bombardelli receiving the Varro Tyler Award

INDENA TAKES PART IN THE MAIN ONCOLOGICAL CONGRESSES

Once again Indena researchers and managers have played an appreciable role at two recent international congresses. At the 228th American Chemical Society National Meeting in Philadelphia, Gabriele Fontana presented groundbreaking research work, focusing on a new class of taxanes with different functionalities in position 14. This new research project was conducted by Indena in conjunction with two important Italian centres, the ISOF Institute for Organic Synthesis and Photoreactivity in Bologna, and Milan University's Marchesini Institute of Organic Chemistry.

"A wide number of 14-functionalized taxoids, generated by this research, have their importance already supported by in vitro and in vivo data, and we will follow the research line pursuing the selection of new candidates", said Dr Fontana.

Indena's oncological research into new taxanes was the subject of two additional studies presented in Philadelphia: these studies follow the route of Ortataxel, a promising paclitaxel analogue at present in phase II clinical studies. This derivative of 14-hydroxybaccatin has stimulated research into new analogues with better chemical-physical features and anti-tumour action.

These, together with new studies into the active principles contained in broccoli, were presented by the Milan-based company Indena during the 95th World Congress on Cancer Research in Orlando. Organised by the American Association on Cancer Research (AACR), this is one of the sector's most important gatherings and attracts an attendance of over 15,000 scientists including oncologists, epidemiologists and researchers from all over the world.

The promising molecules of botanical origin found in broccoli can subsequently be developed into innovative cancer treatment, which is both less invasive and less subject to drug resistance.

A BOOM IN US PATENTS COVERING HERBAL MEDICINE – INDENA IN THE TOP 5 ORGANISATIONS

Undoubtedly, the world market for herbal products is growing in importance. Today alternatives to orthodox medicine are used by more than 80% of citizens in developing countries and by an increasing number of people in developed countries both for general health and wellness. The most prominent application fields are cosmetics, health protectants (nutritional supplements, antioxidants, weight loss etc.) and medicines. This renewed interest in herbal products is mirrored also in research. The US Patent and Trademark Office has recorded an exponential increase in related patents. According to USPTO statistics, 1359 patent applications were filed between 2001 and 2003, a huge number when compared with only 1968 patents granted on botanicals from 1976 to 2003. Relevant news come from the developing



countries, which are now beginning to exploit the commercial potential of traditional knowledge through the intellectual property (IP) protection. In the ranking of top organisations granting the highest number of herbal medicine patents, fourth place goes to Indena.

INDENA COSMETIC SEMINAR IN CHINA

At the same time as Indena attended the 9th International Congress of Dermatology in China, where the anti acne product Sebacin™ was presented, a parallel cosmetic seminar was organised in Beijing on May 19th, following the success of the Ghuangzhou seminar last March. All the main cosmetic companies in the Beijing area were present, with over 80 attendees welcomed at the Gloria Plaza Hotel by Indena representatives and their Chinese distributor Goodway.

Standardized extracts, pure and selected fractions and Phytosome® were illustrated by Jean Marc Laquière, Cosmetic Sales Network Coordinator, while Dr. Aldo Cristoni, Indena's Senior Researcher, focused on products with specific applications, such as anti hair loss, microcirculation and slimming.



Chinese Great Wall

This event reflects the importance Indena gives to the growing cosmetic market in China, says Christian Artaria, Asia Pacific Area Manager, and may serve as a springboard to the creation of technological and development partnerships with Chinese companies.

INDENA REGULATORY SEMINAR IN BRAZIL

As part of Indena's campaign for regulatory assessment and harmonisation, 40 delegates from the Brazilian Ministry of Health gathered in Sao Paulo (Brasil) in May 2004 to hear expert opinions on the subject.

Indena's Quality Assurance Officer, Ernesto Martinelli, conducted the seminar which was entitled: "Indena experience on the quality and consistency of Active Pharmaceutical Ingredients (APIs) of botanical origin according to the current European regulations including Pharmacopoeia, ICH and GMP guidelines". Martinelli underlined how the regulatory activity tended towards global harmonisation of the general rules, including GMP requirements. These affect not only finished products, but crucially, raw materials as well. The quality of active ingredients, making particular reference to botanicals, has become an issue of global importance. Careful monitoring is needed in fact, during several critical stages in the preparation of Herbal products, in order to ensure reproducible quality and a completely safe ingredient.

The Brazilian Health Ministry officials representing the departments of new medicines, dietary supplement, cosmetics, pharmacovigilance, and public health, share a common position on the importance of quality and safety of botanical ingredients.

INDENA HERBALS SEMINAR IN MIAMI

On the occasion of the first Annual Integrative Medicine Conference and Natural Healthcare Expo, held in Miami from 1st to 4th April, Indena offered an educational seminar entitled "Herbals of the new millennium: quality, safety and efficacy".

Attended by around 35 specialists, the Indena seminar addressed the concerns of both General Physicians and Complementary Alternative Medicine Practitioners who prescribe herbal remedies. The Miami seminar

highlighted yet again the importance Indena gives to increasing awareness of quality, safety and efficacy standards.

Scientific Director Paolo Morazzoni, and Edward M. Croom Jr, Adjunct Associate Professor of Pharmacognosy at the University of Mississippi School of Pharmacy, illustrated the development of quality, safety and efficacy criteria for botanical derivatives, presenting an overview of standardisation processes and regulatory issues in Europe, USA and Canada.

INDENA SUPPORTS PARTNERS AND DISTRIBUTORS THROUGHOUT THE WORLD

Last November the first Indena Asian Pacific Regional conference took place in South Korea. As part of our aim to provide maximum support for partners and distributors, who actively promote Indena products, the Scientific Department conducted a number of educational seminars during the gathering in Seoul. These specifically targeted seminars highlighted the features of key products, and included an interesting session on product branding and advertising designed to foster local promotion techniques.

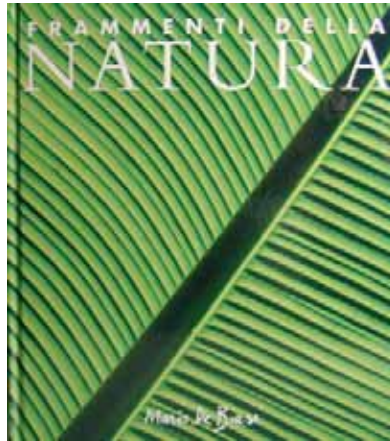


Partners and Distributors participating to the 1st Asia Regional Meeting

“FRAMMENTI DELLA NATURA” BY MARIO DE BIASI: NATURE AS SEEN THROUGH THE EYES OF THE RESEARCHERS AND THE ARTIST

The marvellous images captured by Mario De Biasi's searching gaze and his camera lens reveal what the researching scientific zeal of Indena observes day in day out.

The talent of Mario De Biasi is seen in his singular ability to bring into focus all the secret emotions that lie hidden in a flower, a plant or a tree. Frammenti della Natura (Fragments of Nature) is a work of art which brings together this unique photography with the equally unique focus of Indena amongst the flowers and the leaves, within the plants and the barks of the trees, to pursue the scientific observation of this wondrous spectacle.



Mario De Biasi's book sponsored by Indena

INDENA TO SPONSOR CONFERENCE ON ASSISTANCE FOR PATIENTS

Milan is internationally renowned for its centres of excellence in the treatment of serious illness and disease. Thousands of patients every year are admitted for treatment in city hospitals not only from far-flung Italian regions but also from abroad. Finding lodging for patients and their relatives and carers has become a pressing need in recent years.

Improving the provision of suitable accommodation is the subject of the First Meeting on Patients' Families Hosting Homes, to be held in Milan on 8th November 2004. Organised by a non-profit-making group of charities, co-ordinated by Sodalitas, the meeting will bring together government representatives, religious bodies, doctors, hospital administrators, foundations and social services who provide assistance and accommodation to carers and patients, during and after treatment.

Sponsorship of this conference may be seen as part of Indena's commitment to health care and particularly to the treatment of serious diseases.



A Hosting Home as seen by a young patient

INDENA'S EXHIBITIONS AGENDA

- **Health Ingredients Japan 2004** - Tokyo, Japan
October 5-7, 2004
Tokyo BIG SIGHT Exhibition Center, Stand n. H-B402
- **Health Ingredients Europe 2004** - Amsterdam, The Netherlands
November 16-18, 2004
Amsterdam RAI, Stand n. D14 - Hall 1
- **CPhI 2004** - Brussels, Belgium
December 7-9, 2004
Brussels Expo, Stand n. 7330 - Hall 7
- **Informex 2005** - Las Vegas, Nevada USA
January 17-20, 2005
Sands Expo/Venetian Hotel
- **PCIA - Personal Care Ingredients Asia 2005**
Bangkok, Thailand
March 9-11, 2005
Queen Sirikit National Convention Center, Stand n. 1211
- **In-Cosmetics 2005** - Berlin, Germany
April 12-14, 2005
Messe Berlin, Stand n. D51
- **AACR Meeting** - Anaheim/Orange County, California USA
April 15-20, 2005
- **CPhI Japan** - Tokyo, Japan
April 20-22, 2005
Tokyo BIG SIGHT Exhibition Center
- **Vitafoods International 2005** - Geneva, Switzerland
May 10-12, 2005
Palexpo, Stand n. 140
- **ASCO Meeting** - Orlando, Florida USA
May 14-17, 2005
- **CPhI 2005** - London, UK
November 1-3, 2005
Excel London
- **Supply Side West 2005** - Las Vegas, Nevada USA
November 9-11, 2005
The Venetian & The Sands Expo

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