



Fragrance Industry Shares Latest Research at RIFM INFOX

Held at various spots throughout the world, this year RIFM's Information Exchange (INFOX) was held in its own backyard on May 20, 2004 at the Woodcliff Lake Hilton in New Jersey, USA. A forum for the fragrance industry to exchange information on the latest research on fragrance ingredients, this year's INFOX was attended by more than eighty fragrance industry researchers, developers, and executives.

According to Dr. Ladd W. Smith, President of RIFM, "INFOX was a great success this year and better attended than in the past. I'd like to see RIFM's INFOX grow. It is an excellent learning experience for all involved and the research presented is on the cutting edge for the industry." Next year INFOX will take place in Europe and Japan.

The complete program, as listed here, is available for subscribers to the RIFM Fragrance Ingredients Database in the "What's New" section.



INFOX Program May 20, 2004

Toward more comprehensive research and communication
Dr. Ladd W. Smith, DABT, President, RIFM, Inc., Woodcliff Lake, NJ

Global regulatory requirements and PBT activity: methods, thresholds, significance

Prof. Peter Calow, Roskilde University, Roskilde, Denmark and RIFM Expert Panel Member

Practical application of quantitative risk assessment for sensitizing materials

Dr. Pauline McNamee, The Procter & Gamble Company, Surrey, England

Geranyl nitrile research and other nitrile group considerations

Dr. Anne Marie Api, Scientific Director, RIFM, Inc., Woodcliff Lake, NJ

Hydrolysis of isoegenyl-acetate and eugenyl-acetate by rat and human hepatic microsomes

Dr. I. Glenn Sipes, University of Arizona, College of Medicine, AZ

Role of the FFIDS in global hazard communication

Christen Sachse-Vasquez, Technical Manager, RIFM, Inc., Woodcliff Lake, NJ

Comparison of three simulated respiratory exposures

Daniel Isola, Project Manager - Respiratory Safety, RIFM, Inc., Woodcliff Lake, NJ

Delayed type hypersensitivity to HMPCC and other fragrance materials in a select North American population
Donald V. Belsito, MD, Professor & Director, Dermatology, University of Kansas Medical Center, Kansas City, KS

Association between contact allergy to fragrance mix and other contact allergies

Prof. Magnus Bruze, Malmo University Hospital, Malmo, Sweden

Comparative LLNA results: citral and others of the group of 26

Jon Lalko, Sr. Specialist - Test Program, RIFM, Inc., Woodcliff Lake, NJ



Dr. Pauline McNamee gives her presentation on quantitative risk assessment for sensitizing materials at the 2004 RIFM INFOX

RIFM Scientists Present at Regulatory Seminar in China

Anne Marie Api, Ph.D., RIFM's Scientific Director, and Dr. Ladd W. Smith, DABT, RIFM President, gave presentations on RIFM and its scientific program at the China Association of the Fragrance, Flavors and Cosmetic Industry (CAFFCI) International Seminar on the Regulation of Fragrance & Flavors that took place in Guangzhou, China in March.

Drs. Smith and Api attended CAFFCI's Regulatory Seminar with representatives of IFRA and IOFI. The concerted effort of the three organizations on behalf of the fragrance industry was presented in the context of future interactions with CAFFCI.



From left, Dr. Anne Marie Api, RIFM; Chairman Zhang Dian Yi, CAFFCI; Dr. Matthias Vey, IFRA, Dr. Ladd W. Smith, DABT, RIFM. (Photo provided courtesy of Matthias Vey, IFRA)



From left, Dr. Anne Marie Api, RIFM; Dr. Ladd W. Smith, DABT, RIFM; Dr. Thierry Cachet, IOFI; Dr. Matthias Vey, IFRA; Richard Boncy, IFRA and IOFI. Far right, Prof. Jin Qi Zhang. (Photo provided courtesy of Matthias Vey, IFRA)

CAFFCI Chairman, Zhang Dian Yi, delivered the greeting and a brief introduction of the present situation of the fragrance and flavor industry in China. Professor Jin Qi Zhang introduced the products standard and regulation administration of China's fragrance & flavor industry. Mr. Zhao Tong Gang, Head Officer of the Regulation and Inspection Department of China's Public Health Bureau, discussed related regulations and administration. Mr. Richard Boncy, Executive Director of IOFI and IFRA, presented an overview of the organizations and their roles in regulating the fragrance and flavors industries. Dr. Matthias Vey, Scientific Director of IFRA, and Dr. Thierry Cachet, IOFI Scientific Director, each introduced the structure and code of practice of their respective organizations. Dr. Api and Richard Boncy gave a talk on the relationship between IOFI, IFRA, RIFM and FEMA. Richard Boncy also lectured on the relationship between self-discipline and governmental administration.

Some of the other topics discussed included:

- ◆ Are there any regulations for tobacco in both Europe and USA? Are there any lists of fragrances for tobacco in the world?
- ◆ Maillard Reaction and inspection.
- ◆ Test methods in fragrance and flavored products.
- ◆ The difference in defining natural fragrance between US, Europe and China and identification methods of natural fragrance.

Fragrances can be selected by scent categories, just as you would select a fine bottle of wine.

<i>Floral</i>	<i>Chypre (mossy woods)</i>
<i>Oriental (spicy)</i>	<i>Marine (water or oceanic)</i>
<i>Citrus</i>	<i>Green</i>
<i>Fougère (meaning fern) well-balanced</i>	

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REXPAN News...

R IFM's Expert Panel (REXPAN) held its May meeting in New York City at the Hilton Times Square Hotel.

On May 18th, FEXPAN, the Expert Panel of the Flavor and Extract Manufacturers Association (FEMA) joined REXPAN to discuss data criteria, reproduction protocols and how to appropriately evaluate naturals. This year REXPAN invited Dr. Donald V. Belsito, Professor of Medicine and Director of the Division of Dermatology at the University of Kansas Medical Center in Kansas City, Kansas and Professor Magnus Bruze, Head of the Department of Occupational and Environmental Dermatology at the Malmo University Hospital in Malmo, Sweden, to participate fully in its program during the May meeting. The presence of Dr. Belsito and Professor Bruze added contact dermatitis expertise to the meeting and fostered discussion of European issues, sensitization protocol design and epidemiology information.

Another highlight for the May meeting was dinner with special invitee, Harvey Gedeon, Senior Vice President of Research and Development at The Estee Lauder Companies, Inc. Mr. Gedeon provided perspective for REXPAN on how IFRA Standards impact product formulation, as well as the high value consumer companies place on safe product use.

REXPAN OUTREACH...

Dr. David R. Bickers, Chair of RIFM's Expert Panel, attended the Science, Regulatory and Toxicology Committee meeting of the Cosmetics Toiletries and Fragrance Association (CTFA) on April 17, 2004 in New York City and the 7th European Society of Contact Dermatitis (ESCD) Conference on June 8-11, 2004 in Copenhagen, Sweden.

Dr. Bickers spoke about RIFM's Comprehensive Research Plan and how REXPAN sets its priorities and evaluates data. He also spoke about the areas of professional expertise that were included within the panel. Members are international and cover a range of scientific disciplines that includes toxicology, dermatology, environmental science, and pathology.

Dr. Bickers' visit to Copenhagen and the ESCD conference was part of the effort to widen RIFM's sphere of influence among European colleagues and to communicate the importance of the research RIFM is conducting to ensure the safe use of fragrance ingredients worldwide.

Dr Bickers is the Carl Truman Nelson Professor and Chair of the College of Physicians & Surgeons Department of Dermatology at Columbia University in New York City.

RIFM Holds First Environmental Training Session on Hazard Assessment of Fragrance Materials

R IFM held its first training course on The Hazard Assessment of Fragrance Materials Using the U. S. Environmental Protection Agency's (EPA) Persistence Bioaccumulation and Toxicity (PBT) Profiler. The workshop, for RIFM members, took place in July at RIFM's Woodcliff Lake, N. J. offices.

The PBT Profiler assesses organic chemicals using mathematical models to estimate their persistence, bioaccumulation and toxicity in the environment. It was developed by the EPA in conjunction with the Syracuse Research Corp. Previously, a pilot PBT training program was reviewed by the IFRA Scientific Committee.

Twenty-five member companies were represented, with attendees mainly from regulatory affairs and product safety departments. The training session was offered to distribute the dataset of information developed by RIFM, using the

U.S. EPA's PBT Profiler, on the hazard characterization of fragrance materials. A review of the RIFM environmental program, the PBT Profiler and the RIFM Database were also provided as part of the training. The dataset assessing over 2000 fragrance materials was distributed to the RIFM members who attended the training course.



Training was provided by Dr. Dan Salvito, Manager of RIFM's Environmental Program, and Christen Sachse-Vasquez, Technical Manager of the RIFM Fragrance Materials Database, and was developed in anticipation of forthcoming regulatory challenges addressing the persistence, bioaccumulation and toxicity of chemicals in the environment.

A fall training session in Europe is being planned. RIFM members will be notified by e-mail when a date and location are confirmed.

Donald V. Belsito, M.D. and Professor Magnus Bruze Join RIFM Expert Panel

Donald V. Belsito, M.D. and Professor Magnus Bruze have joined RIFM's Expert Panel (REXPAN); together, they bring to the panel their considerable expertise in contact dermatitis. Dr. Belsito is Professor of Medicine and Director of the Division of Dermatology at the University of Kansas



Dr. Belsito delivering his presentation at RIFM's May 2004 INFOX.

Medical Center, Kansas City, Kansas, USA. His major research interests include occupational dermatoses, contact hypersensitivity, atopic dermatitis, psoriasis, and infectious dermatoses. He received his medical degree from Cornell University Medical College in New York City, completed an internal medicine residency at Case Western Reserve University Hospital and a dermatology residency and fellowship in dermatologic immunology at New York University Medical Center. Dr. Belsito is president of the North American Contact Dermatitis Group, a diplomate of the American Board of Internal Medicine, the American Board of Dermatology (ABD) and the ABD, Special Qualifying Examination in Dermatological Immunology: Diagnostic and Laboratory Immunology. Dr. Belsito is author or coauthor of more than 100 articles published in peer-reviewed journals and more than 30 invited reviews and textbook chapters.

Professor Bruze is Head of the Department of Occupational and Environmental Dermatology at the Malmo University Hospital in Malmö, Sweden. He has been a dermatologist since 1978, specializing in Occupational and Environmental Dermatology since 1981. He completed his Thesis on Contact sensitizers in resins based on phenol and formaldehyde in 1985. Professor Bruze has authored/co-authored some 220 publications, particularly on contact dermatitis and occupational dermatoses.

REXPAN is an independent and international group of dermatologists, pathologists, environmental scientists and toxicologists that advises RIFM on strategic approach, reviews protocols and evaluates all of RIFM's scientific findings. REXPAN's conclusions form the basis for the Standards set by the International Fragrance Association (IFRA).



Professor Bruze speaking from the audience at RIFM's May 2004 INFOX.

RIFM Welcomes New Members

RIFM is pleased to welcome CPL Aromas, Hertfordshire, UK, as an Active Member and The Mary Kay Holding Corp., Dallas, TX, USA and Yves Rocher, Issy les Moulineaux, Cedex, France, as Supporting Members.

Active membership is limited to persons, firms, corporations and divisions of corporations primarily engaged in the manufacture and/or sale or distribution *at other than the retail level* of fragrances or fragrance ingredients. Supporting members are individuals or companies engaged in the manufacture, sale or distribution *at the retail level* of consumer products using or consisting of fragrance or fragrance ingredients.

Scientific Director Celebrates 20 Years With RIFM



Anne Marie Api, Ph. D., RIFM's Scientific Director, is celebrating her 20-year anniversary with RIFM. Hired in 1984 by Dr. Richard Ford, President of RIFM at the time, Dr. Api made a verbal agreement with him to guarantee two years of service. When asked about her longer tenure with RIFM she replied, "I love the work and I love the people."

Coming aboard in 1984 as Scientific Assistant, Dr. Api rose through the ranks to Toxicologist, Manager of Human Health and Safety to Scientific Director, completing her Ph. D. along the way in 1994. Her work over the years was instrumental in making the RIFM/FEMA Materials Database the valuable resource that it has become today.

As Scientific Director, she supervises the planning, conduct, and completion of the research and testing program at RIFM. She is RIFM's liaison to the Expert Panel and to the International Fragrance Association's (IFRA's) Scientific Committee.

from left: Dr Ladd W. Smith, President of RIFM, Dr. Anne Marie Api, Scientific Director of RIFM and Dr. Emil Pfitzer, Past President of RIFM.



Dr. Api keeps a breakneck pace to meet the growing demands for more information on fragrance ingredients and their safe use. Requests for information about RIFM and its work come from all sectors—industry, government, trade associations and the scientific and medical communities. Over the years Dr. Api has become a true road warrior, sometimes logging more time in travel than in the office. She is pictured here on a recent trip to Guangzhou, China to present RIFM's current research and goals.

Dr. Api's professional affiliations include membership in the American Chemical Society, the American Contact Dermatitis Society, the American Management Association, the American Society for Photobiology, the European Society for Contact Dermatitis, the Mid-Atlantic Chapter of the Society of Toxicology, Society of Investigative Dermatology, Society of Toxicology and the Women in Flavor & Fragrance Commerce where she has been a Director on their Board since 1997. She is also a member of the Dermal Clinical Evaluation Society and served on the DCES Board of Directors from 1991-1997.

She has authored over 75 scientific papers.

A luncheon was held in her honor on August 10, 2004 at RIFM headquarters where Dr. Ladd W. Smith, current president of RIFM, presented her with a gold and crystal figurine of a microscope to commemorate the occasion. The luncheon celebration was also attended by Dr. Emil Pfitzer, who served as President of RIFM from 1996-1998.

Did you know that there were formulations for sacred oil and incense recorded in the Bible that mention the work of a perfumer? Look in Exodus 30, 22-38.

RIFM Respiratory Safety Program Highlights

Dan Isola, RIFM's Respiratory Safety Program (RSP) Manager, has spent some of his time making technical presentations in an effort to reach out to some of the organizations whose work impacts or can be effected by RIFM's RSP.

National Candle Association (NCA) and Latin American Candle Manufacturers Association

Isola attended the first World Candle Congress and Trade Show held in Orlando, Florida in April. It was a joint effort between the National Candle Association (NCA) and the Latin American Candle Manufacturers' Association (ALAFAVE).

Blyth, Inc.

Information on RIFM's programs and fragrance ingredients database were disseminated to Blyth, Inc., a candle manufacturer.

Consumer Specialty Products Association (CSPA)

Isola represented RIFM at the CSPA mid-year meeting held in Chicago, IL in May. He gave a brief presentation to the Air Care Division on the planned simulated exposure study of the fragranced candle. If funding can be generated for the study, both CSPA and the NCA have expressed interest in participating. During the Key Issues Committee meeting it was noted that VOC issues are gathering momentum in Europe along with the detergent regulations and the cosmetic directive. The Air Care Division also sponsored a special morning session entitled "The Pluses and Minuses of Naturals." The presenters offered different perspectives on natural household products and biobased products (A biobased product is made from seeds or plant oils). Natural and synthetic waxes were compared as well as fragrance materials.

Indoor Air Quality Paper

A white paper was prepared on indoor air quality. Based in part as a result of Dan Isola's visit in January with the German Federal Environment Agency, Umweltbundesamt (UBA), the paper is available from the News and Events section of the RIFM web site at www.rifm.org.

International Life Sciences Institute/Health and Environmental Sciences Institute (ILSI/HESI) Workshop

The ILSI/HESI workshop on respiratory hypersensitivity took place on June 3-4, 2004, in Washington, D.C., focusing mainly on pharmaceuticals and isocyanates with relevant discussions on issues addressed by the Respiratory Safety Program. They included:

- The relationship between respiratory allergy caused by low molecular weight materials and IgE.
- Respiratory endpoints of respiration rate, tidal volume, inspiration and expiration times breathing patterns, and peak expiratory flow rates. Other endpoints discussed

were cytokine levels, antibodies, and cell types.

- Dermal allergens that can not automatically be classified as respiratory sensitizers.
- Respiratory sensitization defined by elicitation rather than induction and the lung's greater potential to generate an immune response.
- Differences in T-cell responses in dermal and respiratory allergy.
- Cytokine fingerprinting used as an approach to safety assessments.

Environmental Protection Agency (EPA)

Dan Isola met with Mark Mason of EPA's Indoor Environment Management Branch. The purpose of the meeting was to correct a misinterpretation of a recent paper posted on the web site for Environmental Science and Technology entitled "Full Scale Chamber Investigation and Simulation of Air Freshener Emissions in the Presence of Ozone" by Liu, *et al.* Mason was the primary investigator for the study that suggested plug-in air fresheners may be a source of VOCs. Another web site published a summary of the paper but the interpretation of the data was incorrect and was refuted by both the CSPA and FMA. Because the Respiratory Safety Program at RIFM conducted its own study on a surrogate plug-in air freshener, Isola wanted to share his findings with Mason.

Generally, Mason said the study was not intended to be an indictment against plug-in air fresheners. The goals of the study were to characterize emission sources, characterize reaction products, conduct particle size analysis on the reactants, and develop models to study indoor air quality. Mason said more data were needed. EPA issued 2 press releases stating that the study was not intended to assess the safety of indoor air fresheners and that the study was misinterpreted. In addition, the CSPA president commented that plug-ins are tested and safe and they are subject to the Consumer Product Safety Commission (CPSC) regulations.

National Institute of Occupational Safety and Health (NIOSH)

Dan Isola attended a NIOSH sponsored workshop on Indoor Chemistry and Health held at the University of California, Santa Cruz, from July 12-15. The goal of the workshop was to address the components of indoor air reaction products and how they affect human health. The majority of the presentations were on indoor air chemistry, rather than health and stressed the importance of reaction products such as free radicals and other short-lived reactive species. A key concern was the presence of ozone in indoor air and the spreading use of ozone generators. Ozone is a major cause of reaction products in indoor air. In addition,

ozone is a lung irritant and the EPA recommends against using ozone generators.

Presentations, Posters and Publications

1. Isola, D. A., Rogers, R. E., Ansari, R. and Smith, L. W. Exposure characterization from a surrogate fine fragrance. The Society of Toxicology in Baltimore, Maryland.
2. Cortes, D.R., Isola, D. A., Ansari, R., Black, M. S. and Smith, L.W. Characterization of fragrance exposure concentrations and temporal trends from a plug-in air freshener. The American Industrial Hygiene Association Conference and Exhibition in Atlanta, Georgia.
3. Smith, L. W., Rogers, R., Black, M. S. and Isola, D. I. Exposure characterizations of three fragranced products. The International Congress of Toxicology in Tampere, Finland.

Posters of the respiratory safety study presentations 1. and 3. listed above are available from RIFM in 11" x 17" printed format or electronically in .pdf format. To request a poster, contact Dan Isola at disola@rifm.org.

Look for upcoming presentations at

- The American Association for Aerosol Research in Atlanta, Georgia, October 4-8, 2004.
- The American College of Toxicology in Palm Springs, California, November 7-10, 2004.

Publication of the pressurized aerosol air freshener simulated exposure study and the plug-in heated oil air freshener simulated exposure study are presently underway.

RIFM Staff Software Training Leads to Database Efficiencies

The RIFM and participating FEMA staff received Alchemy Software training during the month of June. Alchemy document management software is the secure digital archive that RIFM uses to house all of its 41,000 plus, and growing, articles that comprise the references in the RIFM/FEMA database. A certified instructor from Information Management Research (IMR), the company that designed Alchemy, visited RIFM offices and brought the staff up to speed on new advances and improved ways to use Alchemy.

In June, RIFM also started subscribing to Alchemy Web, an Internet viewer that interfaces with the Alchemy digital archive. All articles are now available on the Internet for use by RIFM off-site technical consultants and designated FEMA staff. Authorized users are able to view, print and download articles directly from the website for ease of use. Alchemy Web 4.0 is one of the most secure products on the market because documents are encrypted and cannot be accessed outside of the program's secure viewer. Moreover, no temporary copies are stored on the user's computer.

The results of the training are faster processing of documents into the digital archive enabling more information to be entered into the RIFM/FEMA database in less time.

RIFM's President and Scientific Director Appointed Faculty Status at UMDNJ

President of RIFM, Dr. Ladd W. Smith, DABT, and Dr. Anne Marie Api, Scientific Director of RIFM were both appointed as Adjunct Assistant Professors at the University of Medicine and Dentistry of New Jersey (UMDNJ), School of Health Related Professionals, Department of Clinical Laboratory Sciences on April 20, 2004

For the last several years, Drs. Smith and Api have recruited summer interns for RIFM by giving lectures to the toxicology classes at UMDNJ. This year's lecture was given

on March 15. The adjunct faculty appointments were a result of their involvement with this program.

This year's interns, Maria Mendonca and Christopher Namendorf., are preparing sensitization summary tables and drafting Fragrance Materials Reviews (FMRs) and helping RIFM staff to complete the next group summary on cinnamic acid and related fragrance materials soon to be published in *Food and Chemical Toxicology*. Their internships with RIFM contribute to the completion of their degree programs in Toxicology at UMDNJ.

Article Reprints and Poster Handouts Available from RIFM

Posters

A sensitization safety evaluation for HMPCC (Lyrall). A.M. Api. 43rd Annual Meeting of the Society of Toxicology, 21-25 March 2004, Baltimore, MD.

Photomutagenicity of bergamottin and isopimpinellin. J. Cocchiara and A.M. Api. 43rd Annual Meeting of the Society of Toxicology, 21-25 March 2004, Baltimore, MD.

Simulated exposure to a surrogate fine fragrance. D.A. Isola and L.W. Smith. 43rd Annual Meeting of the Society of Toxicology, 21-25 March 2004, Baltimore, MD.

LLNAs of essential oils/natural extracts. J. Lalko and A.M. Api. 43rd Annual Meeting of the Society of Toxicology, 21-25 March 2004, Baltimore, MD.

Developmental toxicity of acetyl cedrene. A. Lapczynski, J. Cocchiara, D.A. Isola, A.M. Api. 43rd Annual Meeting of the Society of Toxicology, 21-25 March 2004, Baltimore, MD.

Developmental toxicity of OTNE. C.S. Letizia, J. Cocchiara, D.A. Isola, A.M. Api. 43rd Annual Meeting of the Society of Toxicology, 21-25 March 2004, Baltimore, MD.

The Importance of applying "clean" and validated quantification techniques for studying environmental levels of materials used by consumers. D.T. Salvito, R. Kallenborn, H.E. Allen, and P. Chiu. Society of Environmental Toxicology and Chemistry 14th Annual European Meeting, 18-22 April 2004, Prague, Czech Republic.

Exposure characterizations of three fragranced products. L.W. Smith, R. Rogers, M.S. Black, and D.I. Isola. ICTX Congress, 11-15 July 2004, Tampere, Finland.

Papers

Dissipation of fragrance materials in sludge-amended soils (2004). Difrancesco A.M., Chiu P.C., Standley L.J., Allen H.E. and Salvito D.T. *Environmental Science and Technology*, 38(1), 194-201.

Ethanol and diethyl phthalate: vehicle effects in the local lymph node assay. 2004. Lalko, J., Isola, D. and Api, A.M. *International Journal of Toxicology*, 23(3), 171-177.

Evaluation of the oral subchronic toxicity of AHTN (7-Acetyl-1,1,3,4,4,6-hexamethyl-1,2,3,4-tetrahydronaphthalene) in the rat. (2004). Api A.M., Smith R.L., Pipino S., Marcylo T. and De Matteis F. *Food and Chemical Toxicology*, 42, 791-801.

Fragrance materials and their environmental impact. (2004) D.T. Salvito, M.G. H. Vey, and R.J. Senna. *Flavor and Fragrance Journal*, 19:105-108.

To receive any of the posters or papers listed above or for any others not listed here, please e-mail rifm@rifm.org. For posters, please specify if you would like to receive it as a printed copy or if you would like it sent to you electronically as a pdf. Papers are available only in printed form.

Sandalwood is so precious that it is produced under government supervision, mainly in the East Indian province of Mysore. The trees must grow for 30 years and to a height of approximately 10 feet before the oil is fully mature.

The Damasc Rose blooms for just 30 days each year and they are still picked by hand in a race against time. As the day warms up, the blossoms begin to lose their bite and by noon they are only half as rich.

Believed to have originated in Asia, lemons made their way to Europe via Sicily. It takes about 1000 lemons to yield 1lb of oil.