INTERNATIONAL CENTRE FOR SCIENCE AND HIGH TECHNOLOGY

in cooperation with
Chemistry Department, Moscow State University

Aide-Memoire

of the

Workshop on
" Combinatorial Chemistry and Combinatorial Technologies"

13–14 May 2004

Moscow, Russia

Organized
in Cooperation with
CEI – Central Europe Initiative

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

1. Background

The development of new drugs, pharmaceuticals, pesticides, food additives, cosmetics, polymers, catalysts, and materials with brand new properties probably represents the goal of the chemical industry in the new millennium. In the past, the traditional chemical methods implied the design and synthesis of individual new compounds. Subsequently, the promising ones were selected by elaborate screening procedures, then chemists resorted to one by one synthesis of variants of the parent compound. After the introduction of combinatorial chemistry and high-throughput screening, this scenario became obsolete. Molecular diversity — the "product" of combinatorial chemistry — can be easily achieved by one of the two main approaches: (i) split–mix strategy or (ii) the parallel synthetic strategy. To exploit the inherent efficiency of either approach, recently, highly sophisticated robotic systems are widely used.

Combinatorial chemistry has turned traditional chemistry upside down. It requires chemists to think not in terms of synthesising single, well-characterised compounds, but in terms of simultaneously synthesising large populations of compounds. It also requires that those involved with information management and computational chemistry systems address the same issues as the chemists.

Although main emphasis today is on use of combinatorial methods in pharmaceutical applications: the technique is suitable whenever a high number of compounds have to be prepared for testing. Additional fields include agro research, material research, etc. Most major pharmaceutical companies are active in the field, and it is generally accepted that the methods have high potential for the so-called lead finding and drug discovery process: the technology is expected to contribute to the reduction in time and costs.

A lack of co-ordinated effort in developing countries has meant that CC/T and MD have not been channelled into programmes of industrial development. Developing countries (some African countries, Argentina, Brazil, China, India, Indonesia, Malaysia, Mexico, Philippines, Thailand, etc.) and countries of Central and East Europe are strongly aware of their need to take up combinatorial technologies. These are indeed vital to local enterprises if they are to remain competitive and economically viable in the coming decades, and for gaining expertise on application practice in combinatorial technology.

The International Centre for Science and High Technology (ICS) is an autonomous institution within the legal framework of the United Nations Industrial Development Organization (UNIDO), with headquarters in Trieste, Italy.

The ICS mandate relates to know-how transfer and technology transfer from developed countries to developing countries, and derives its justification from the perception that a competitive industrial and technological capability cannot be built-up without an adequate scientific knowledge and without participating in the development and utilization of new and advanced technologies.

In this present workshop programme, the ICS’s activities focus to the diverse field of combinatorial science in order to strengthen the links between academy and industry. Further objective of the workshop is to provide advanced training to post-doctoral level persons interested in the latest developments of the combinatorial technologies. In selecting the specific subprogrammes and their related activities special consideration are given to their relevance in relation to the scientific and technological development of developing countries.

2. Justification

Combinatorial methods can be used whenever high numbers of compounds have to be prepared for testing. The pharmaceutical industry has passed through a remarkable transition in the last few years and much effort was done to identify novel targets in order to find new, therapeuticlly useful compounds by using the tools of combinatorial technology. Although the major pharmaceutical companies in Central Eastern Europe made the initial steps toward the introduction of the combinatorial approach in their research projects, still they are lagging behind the leading companies. The demand for new materials with defined functions, e.g. polymers, catalysts, pigments, liquid crystals, superconductors, thermo- and photochromic materials, to mention a few, has been increasing continuously. Combinatorial chemistry has a great potential to accelerate the process which leads to the discovery of such novel materials.

Economical reforms in the Russian Federation caused significant changes in pharmaceutical industry and related fields. Many factories which early produced pharmaceutical substances have not survived, and imported substances start to dominate at the Russian market. The governmental support

strongly stimulates producing of domestic pharmaceutical substances, however, the lack of investments lead to the predominance of generics versus original drugs. Currently the situation is slowly improving due to formation of state unitary enterprises (GUPs) which join academic institutions and industrial plants in a sort of state-controlled holdings. However, such novel big pharmaceutical units are only partially interested in the long-terms projects related to combinatorial chemistry and drug design. Independent private eneterprises are still oriented to generic production, although they are also provide slowly growing interest to the CC-CT topics.

Second trend which deeply involve academic researchers to the projects related to combinatorial chemistry and combinatorial technologies is the fast growth of small and medium size companies which produce large libraries of screening compounds. Starting from middle 90s several such companies (ChemBridge, Asinex, ChemDiv, InterBioscreen etc.) have quickly grown up and established their own laboratories in Moscow and other places. Such laboratories are well-equipped and require highly qualified personnel. Therefore, there is a growing need of qualified researchers with strong background in the field of combinatorial chemistry. Such companies quite frequently offer support for local academic institutions and universities sponsoring scientific meetings, olimpiads, exhibitions etc.

Chemistry department of Moscow State University flexibly reflects the above trends in the research area, teaching projects, and interaction with combichem-oriented business sector. Starting from late 90s the new speciality "Medicinal chemistry" has appeared due to the initiative of academician Zefirov, and the respective medicinal chemistry course has been started for undergraduate students. The Chemistry department is the birthplace of the special practical course on combinatorial chemistry. The course was launched by the group of Dr. Babaev in 2000 for the students of the last year of education. During last three years about 50 students have received practical education on the topics (1) of combinatorial database creation and manipulations, (2) liquid-phase parallel synthesis, and (3) basic principles and elementary technique of solid phase synthesis. The number of diplom works and PhD topics devoted to computer-assisted drug design, preparation and screening of target libraries, first domestic research on solid phase heterocyclic synthesis is quickly growing during the last 4 years.

An interest of western pharmaceutical companies in deeper interaction with Russian chemists has resulted in the organization of the series of workshops (2002-2004) sponsored by Innocentive company (USA), hosted by the Chemistry Department and chaired by academician Lunin. Additional significant efforts have been performed by the Chemistry department to keep the traditions of high-level national scientific meetings. In total 10 scientific events for last 4 years have been organized by the department. Series of symposia on organic synthesis (1999, 2001, 2002, 2004 organized and chaired by academicians Zefirov, Beletskaya, and Dr. Babaev in Zvenigorod, Yaroslavl' and Uglich) involved CC-CT topics as an integral part. Furthermore, specific conference devoted to CC-CT topics launched by MSU have become traditional. Thus, national meetings on combinatorial chemistry (2002, 2003) and so-called EuroAsian meetings on heterocycles in combinatorial chemistry (organized by MSU in 2000, 2004, 2004 in the university campus, Zelinskii institute of organic chemistry in Moscow, Suzdal, Novgorod, Novosibirsk and chaired by Dr. Babaev) served as a link between academic and industrial researches from East and West.

Recently built novel Center of Molecular Medicine of MSU houses research groups and some industrial groups involved in combinatorial chemistry. A recent project (MSU - Chembridge) implies investment of the company for expenditure building of the novel Center of combinatorial chemictry.

3. Objectives

Following the recommendations of the steering committee of ICS-UNIDO an event has been organised in cooperation with the Department of Chemistry of Moscow State University on May 13-14 15–18, 2004.

This meeting is addressed to participants from academy, industry and R&D institutions from Russia and CIS countries. The main objectives of the workshop are:

- To evaluate the state of the art of combinatorial chemistry and combinatorial technology and their industrial applications in Russia and CIS.
- To build awareness among industry and academic partners on a very rapid development of combinatorial chemistry and its relevance for industry in the region.

- To identify regional R&D institutions in Russia and through contacts establish with the participants in the workshop.
- To give ICS an opportunity of identifying qualified centres to be considered as future cooperative institution for the ICS network.
- To evaluate possible initiatives (as follow-up projects and feasibility studies) of industry and academy concerning combinatorial chemistry from Russia and CIS countries.
- To set up a regional ICS-UNIDO network on Combinatorial Chemistry and Combinatorial Technology.

4. Outputs

- To advance the scientific and technological level of participants in the field of Combinatorial Chemistry and Combinatorial Technologies.
- Preliminary proposals of follow-up projects of feasibility studies for the implementation of combinatorial chemistry in chemical research and innovation.
- Identification of possible cooperative institutions in the relevant field.

5. Profile of Participants

The workshop is intended for scientists, industrialists, and technologists in the following areas: chemistry, medicinal chemistry, pharmaceutical industry, agrochemistry, and materials science. It is supposed that the core audience of the event will involve the deans of chemistry departments of Russian educational institutes (universities, technical and pedagogical universities) capable to assist administratively the implementation of CC-CT knowledges in their domestic institutions in the form of educational, scientific, and industrial projects. Another prefered category of participants would be the applicants from Russia and CIS countries who actively participate in their countries programme on research and industrial application of combinatorial science and combinatorial technology or who are involved in the implementation of such programmes. As the course will be conducted in English, participants should have an adequate working knowledge of that language.

6. Tentative Programme

Workshop (2 days)

- UNIDO CC-CT program
- Solid phase synthesis in drug discovery
- Introduction to design of combinatorial libraries
- Solid phase preparation of peptides and polycondensed heterocycles
- Solid phase heterocyclic synthesis
- Teaching students the combinatorial chemistry
- Automated synthesis using domestic equipment
- Throughput screening
- Dynamic combinatorial libraries
- Combinatorial investigation applied to heterogeneous catalysis
- Microwave applications in combinatorial chemistry and high throughput synthesis
- High-throughput analytical methods for library characterization
- Round tables
- Regional/country reports
- *Practical demonstration of Syncore parallel synthesis/filtration reactor at MSU*
- *Equipment/software exhibition*
- Excursion to Chembridge laboratories

7. Documentation

The basic documentation of the workshop will consist of:

- List of participants
- Aide Memoire
- List of speakers

- Abstracts of contributions and of the presented materials will be distributed during the event

8. Time and Venue

The Workshop *Combinatorial Chemistry and Combinatorial Technologies* will be held on May 13–14, 2004. The event will be hosted by the Department of Chemistry of Moscow State University.

9. Language

The official language of the workshop will be English.

10. Financial/Administrative Arrangements of ICS-UNIDO financed participants

For participants from Russia the round-trip economy air tickets or train tickets will be reimbursed for the most direct and economical route.

For invited participants of the meeting from abroad the round-trip economy air tickets or international train tickets will be reimbursed for the most direct and economical route.

Foreign participants will be required to bear the costs of all expenses in their home country incidental to travel abroad, including expenditure for passport, visa, and any other miscellaneous items as well as internal travel to and from the international airport of departure in their home country.

The organization will not be responsible for any of the following costs, which may be incurred by the participants while attending the training course:

- compensation for salary or related allowances during the period of the meeting;
- any cost incurred with respect to insurance, medical bills and hospitalization fees;
- compensation in the event of death, disability or illness;
- loss or damage to personal property of participants while attending the events.

11. Visa Arrangements

Foreign participants are requested to arrange for their visa, if required, as early as possible at the Embassy in their home country. In case of difficulties, please advise the contact persons mentioned below.

12. Registration and Contact Persons

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