Workshop Programme

New Safe Medicines Faster

March 15-16 ● 2000 ● Le Plaza ● Brussels ● Belgium

Wednesday, March 15, 2000 – Memling Room

12.30	**Welcome and opening address** *Prof. Malcolm Rowland, EUFEPS President, Manchester, UK* *Mr Bruno Hansen, Director of Life Sciences – Coordination, The European Commission* **The New Safe Medicines Faster Initiative** *Prof. Ole J. Bjerrum, Chair Organising Committee, Bagsvaerd, DK*
13.00	**LECTURE SESSION I** *Chair: Prof. Ole J. Bjerrum, Bagsvaerd, DK*
13.00 – 13.35	**How to select candidate drugs faster?** *Prof. Trevor Jones, London, UK*
13.35 – 14.10	**How to bring candidate drugs faster into human?** *Dr Frank Fildes, Macclesfield, UK*
14.10 – 14.45	**How to bring candidate drugs faster into full-scale production?** *Prof. Staffan Folestad Mölndal, SE*
14.45 – 15.15	Coffee/tea break
15.15	**LECTURE SESSION II** *Chair: Dr Jürgen Reden, Brussels, BE*
15.15 – 15.50	**How to bring drugs faster to regulatory acceptance?** *Dr Brian White-Guay, Brussels, BE*
15.50 – 16.25	**How to streamline the drug development process?** *Prof. Fritz Bühler, Basel, CH*
16.25 – 17.00	**How to utilise IT to speed-up the drug development process?** *Dr Alistair Shearin, London, UK*
17.00 – 17.35	**How to bring new biotech molecules into deliverable products?** *Prof. Daan Crommelin, Utrecht, NL*
17.35 – 18.00	**Organisation of Workshop Sessions** *Prof. Ole J. Bjerrum, Bagsvaerd, DK*
20.00 –	**Reception & Dinner**

Thursday morning, March 16, 2000 – Break-out Rooms

08.30 – 11.30 **PARALLEL WORKSHOP SESSIONS**

Session 1 **How to select candidate drugs faster?**
Room: *Chair:* *Prof. Trevor Jones, London, UK*
Memling *Co-chair:* *Dr Pia Vuorela, Helsinki, FI*
Rapporteur: Assoc. Prof. Maj-Inger Nilsson, Brussels, BE

Session 2 **How to bring candidate drugs faster into human?**
Room: *Chair:* *Dr Frank Fildes, Macclesfield, UK*
Paola *Co-chair:* *Prof. Theodor W. Guentert, Basel, CH*
Rapporteur: Prof. Sven Froekjaer, Copenhagen, DK

Session 3 **How to bring candidate drugs faster into full-scale production?**
Room: *Chair:* *Prof. Staffan Folestad, Mölndal, SE*
Louise-Marie *Co-chair:* *Prof. Henk de Jong, Courbevoie, FR*
Rapporteur: Prof. Jörgen Vessman, Mölndal, SE

Session 4 **How to bring drugs faster to regulatory acceptance?**
Room: *Chair:* *Dr Brian White-Guay, Brussels, BE*
Astrid *Co-chair:* *Dr Christian Kalcher, Vienna, AU*
Rapporteur: Dr Jan Renneberg, Copenhagen, DK

Session 5 **How to streamline the drug development process**?
Room: *Chair:* *Prof. Fritz Bühler, Basel, CH*
Elisabeth *Co-chair:* *Dr Graham Hughes, London, UK*
Rapporteur: Dr Jürgen Reden, Brussels, BE

Session 6 **How to utilise IT to speed-up the drug development process?**
Room: *Chair:* *Dr Alistair Shearin, London, UK*
Fabiola *Co-chair:* *Dr Enzo Grossi, Milan, IT*
Rapporteur: Prof. Göran Alderborn, Uppsala, SE

Session 7 **How to bring new biotech molecules into deliverable products?**
Room: *Chair:* *Prof. Daan Crommelin, Utrecht, NL*
M-Henriette *Co-chair:* *Prof. Manuel Carrondo, Oeiras, PT*
Rapporteur: Prof. Claus-Michael Lehr, Saarbrücken, DE

(Coffee/tea would be available at 10 a.m.)

12:00 Lunch

Thursday afternoon, March 16, 2000 – Memling Room

13.00 – 14.40 **PLENARY FEED-BACK REPORT SESSION**
Chair: Prof. Trevor Jones, London, UK
Co-Chair: Assoc. Prof. Anders Grahnén, Uppsala, SE

Workshop Session 1
Rapporteur: Assoc. Prof. Maj-Inger Nilsson, Brussels, BE

Workshop Session 2
Rapporteur: Prof. Sven Froekjaer, Copenhagen, DK

Thursday afternoon, March 16, 2000 – Memling Room - Continued

Workshop Session 3
Rapporteur: Prof. Jörgen Vessman, Mölndal, SE

Workshop Session 4
Rapporteur: Dr Jan Renneberg, Copenhagen, DK

Workshop Session 5
Rapporteur: Dr Jürgen Reden, Brussels, BE

Workshop Session 6
Rapporteur: Prof. Göran Alderborn, Uppsala, SE

Workshop Session 7
Rapporteur: Prof. Claus-Michael Lehr, Saarbrücken, DE

14.40 – 15.00 Coffee/tea

15.00 – 16.15 **Report Session continued: General Discussion**
Chair: Prof. Malcolm Rowland, UK
Co-Chair: Prof. Daan Crommelin, Utrecht, NL

16.15 – 17.00 **Summary, conclusions and closing remarks**
Dr Jürgen Reden, EFPIA, Brussels, BE
Dr Jan Renneberg, Danish Medicines Agency, Copenhagen, DK
Prof. Malcolm Rowland, EUFEPS, Manchester, UK
Prof. Ole J. Bjerrum, Chair Organising Committee, Bagsvaerd, DK

17.00 ***Closing of the Workshop***

How to bring candidate drugs faster into full-scale production?

Prof. Staffan Folestad, AstraZeneca R&D, Mölndal, Sweden

Background. Based on innovative and successful R&D, the European pharmaceutical industry built itself a strong business position during the second half of the last century, also when compared to global measures. This is evident not the least from the number of new treatments that have been provided by European companies. Indeed, not only have they introduced pharmacotherapy for diseases where there previously either was a lack of treatment or where drugs were only available for relief of symptoms, but also this research and development has added other values to patients and society. New drug products have for example been developed that reduce or even omit the need for hospitalisation or surgery. Other product examples are those based on drug delivery systems that optimise the therapeutic plasma drug concentration profile over time thereby yielding good temporal control. This is also beneficial in that the administration frequency is reduced from several times per day to once-daily (e.g., oral modified release formulations) and once-monthly or even longer (e.g. parenteral depot formulations). Additionally, it has also been demonstrated that in this way patient compliance can be significantly improved. In all, this emphasise that drug product development is a combined result of advanced R&D not only within Drug Design and Medicinal Chemistry but also within Drug Delivery and Pharmaceutical Technology.

Currently, the pharmaceutical industry is facing challenges from a changing health care environment, for example the gradual ageing of the population in the developed world. In addition, increased expectations from the society of reduced costs for treatments have put a focus both on the cost-effectiveness of therapies and on direct drug purchase costs. On the other hand, development of new medicines requires that industry in parallel must deal with increases in R&D investments needed that are typical for development of any innovative and advanced product. Notably, the European pharmaceutical industry shares its general situation with the EU chemical industry in that the proportion of sales devoted to R&D was trending upwards until 1993 when it flattened out. Indeed, in this respect Japan has taken over the lead from the EU since 1991.

In this context, it is obvious that re-examination of the entire R&D process should serve as an introductory step to secure a long-term competitive position for drug development in Europe.

Aim of introductory lecture. The aim of this paper is to critically examine the development route from selected CD to full-scale commercial production. It will comprise characterisation of the role of current technologies used to support this process and pay special attention to rate-limiting steps. Moreover, a screening will be included of potential key technologies of the future that could support development of new, safe medicines faster. In addition, the necessary R&D to develop these as well as shared responsibilities needed between academia and industry will be addressed.

Characteristics of current development/manufacturing processes. The development time for a pharmaceutical product is generally long compared to other industrial products. Here, the device, “a drug is more than a molecule,” is central for understanding the specific conditions under which this development is conducted. After the discovery phase, during which the active drug compound is identified, drug delivery must be optimised in order to facilitate optimal and safe administration of the active compound to the patient. At this stage, i.e. after the CD has been selected, product development requires that adequate preformulation data are available. Such data then constitute the scientific basis from which the drug is formulated into a dosage form having optimal biopharmaceutical characteristics. Typical finished products comprise the drug compound in a vehicle such as a tablet, a capsule, an injection solution, or a spray device. Traditionally these are manufactured by a series of unit operations that comprise batch processes, e.g. synthesis, blending, coating and tabletting. A high product quality is then secured through appropriate processing as verified by comprehensive sets of test methods. A critical part of the testing during development is stability testing that aim at securing drug potency, functionality etc. over time so that a sufficient shelf lifetime is obtained for the finished product.

Because of the complexity and high quality demands on pharmaceutical products, development of the formulation or preparation and related manufacturing processes require a vast amount of “system thinking.” In all, this emphasise that it is essential to get the most out of as few experiments as possible. Indeed, this has been the driver for promoting the introduction of experimental design in recent years. Although currently used most frequently for optimising primary production processes it is becoming more widely in use also for secondary production processes. Moreover, experimental design has been shown to be particularly useful during upscaling and process validation as a means to identify control regions for robust operation of the manufacturing processes. In this way product quality is optimised while safe tech transfer is supported from the R&D site to the commercial production site.

In parallel with product development, analytical development is a laborious and time-consuming task. Not only shall it support development of the product ***per se*** but it must also generate the necessary set of test methods to be used in the commercial production for release of product batches. Because of regulatory requirements, the width and burden of testing has continuously increased during the last decades. Notably, testing is so far predominantly carried out in the QC lab although parametric release, i.e. release based on in-process tests, has been discussed as an alternative. Indeed, increased efforts, particularly among major business actors, are currently focused on developing more thorough schemes for in-process testing.

Strategies and key technologies. The following section is an outline along what lines solutions could be sought in order to enable a faster development process from CD to full-scale production. However, it should be noted that it is neither a complete inventory nor a comprehensive review of future key technologies, the intention is rather to share a few personal views that might serve as a starting point for a more thorough inventory in the succeeding workshop.

A first reflection concerns the increased gap regarding use of novel technologies during drug development that can be noted between major and small business actors. Indeed, megabrands and global introduction of new drug products are already strong drivers for the major companies to implement such technologies when they are considered to add value to the development process. In this respect, the route from CD to full-scale production may already be characterised to be more or less “lean development.” Thus, because the actual working process inevitably is different between different companies, internal bottlenecks, rate-limiting and weak steps may be somewhat different.

The second reflection concerns the impressions that the preceding discovery phase is characterised primarily by development on a molecular level whereas concept testing, process development and up-scaling is a mix between characterisation on a molecular level and a more traditional empirical working process. Indeed, the author is convinced that any progress that can strengthened the development with respect to work predominantly on a "molecular level" also during product development would be beneficial. For example, in this way the shortest path from construction to full-scale manufacturing could be reliably predicted. Requirements for site-specific stability data might also be reduced and the basis for release of commercial batches could be moved from post testing to process measurements.

The direct implication of a "molecular approach" from CD to full-scale processing is that it places analytical chemistry and measurements in focus as well as their impact on process system engineering. In recent years new possibilities for accomplishing analytical chemistry in real-time have received increased attention. When applied to industrial manufacturing processes, this is commonly referred to as Process Analytical Chemistry (PAC). The basis for this progress is the rapid development within fields such as optronics, computer technology, and not the least, development of methods for extracting information from complex data matrices, e.g., chemometrics and data mining. In particular, physico-chemical properties of products or process intermediates may now even be measured non-invasively and non-destructively by means of spectroscopic techniques such as NIR and Raman. Moreover, these techniques also permit quantitative analysis of solid samples such as powders, tablets and capsules. These contrasts with traditional test methods where the analysis is predominantly conducted in solution, e.g., dissolution testing and assays based on liquid chromatography (HPLC). Indeed, important solid state properties of tablet, granule and powder samples are thereby lost. Still, perhaps the most challenging aspect of this progress is the new possibilities for measurements in direct connection with manufacturing processes (at-line analysis) or even inside the chemical processes (in-line analysis).

By carrying out measurements at-line or on-/in-line in these processes, deviations from desired behaviour can be identified at an early stage which not only minimises the risk for rejecting batches during commercial production but even more rewarding, also makes process development controllable on a molecular level. Noteworthy, such process sensors can be used either for direct control of the process and/or for generating QC data. It follows that such technologies introduce a paradigm shift for development and manufacturing of drug products because they can actually provide direct information of product attributes. In a broader perspective, with a developed strategy for process measurement as part of the overall quality control, traditional QC testing on the finished product can be made redundant. That is, it opens possibilities for release of commercial batches even of solid dosage forms where the assurance that the product is of the intended quality is based solely on information collected during the manufacturing process, i.e., "Parametric Release." In all, this emphasises the importance of development of PAC in general, and that PAC is not only a matter of interfacing analysers to manufacturing processes but is a holistic approach towards more in-depth knowledge of process chemistry.

Research needs. Progress to enable product development, up-scaling and full-scale production on a "molecular level" require interdisciplinary research and technical development at the highest scientific level. Work along this direction is already ongoing at some European universities, research centres and some industry actors. However, it is fair to conclude that neither of these activities may provide the necessary complete scientific platform for the European pharmaceutical industry to benefit from. Indeed, there is so far no concerted EU initiative taken for such an interdisciplinary RTD program, albeit tentative collaborators with the right scientific competence can be identified.

How to bring drugs faster to regulatory acceptance?

Dr Brian White-Guay, Merck Sharpe & Dohme Europe, Brussels, Belgium

It is generally acknowledged that the main objectives of a regulatory system with regards to medicinal products should have as fundamental aim to ensure protection of public health by instituting or fostering: an efficient and rapid approval system for products shown to be effective and safe within the context of use, an efficient and rapid approval system for clinical trials of investigational drugs with appropriate protection of human subjects, clear standards of drug quality with appropriate controls of manufacturing, effective post-marketing surveillance which allow timely updating of safety information, measures to stop distribution of unsafe products, an environment that encourages robust drug development programs and last but not least transparency of the evaluation and decision making process. To this effect, it is expected that there should be an on-going program aimed at developing new scientific methods and new regulatory testing paradigms to assure the identity, quality, safety, and effectiveness of human drug products in addition to a dedicated effort in providing scientific support for the development and application of regulatory policy and decision-making .The European Commission should through it's institutions and in collaboration with Member States initiate a dedicated program to conduct and co-ordinate applied drug research that converts new scientific knowledge to regulatory applications. The purpose of this workshop will be to explore potential topics and avenues that could better serve this objective in light of the current experience and formulate recommendations for the next RTD Framework programme.

How to streamline the drug development process?

Prof. Fritz R. Bühler, University Hospital, Basel, Switzerland

Proof of Concept may become a pivotal decision point (phase I/IIa) in the early clinical development of medicines, which shifts from process-based frontloading to science-driven frontloading and novel information management and decision making. Proof of Concept is based on scientifically sound evidence to support mechanism of action (biomarker, surrogate endpoint or clinical assessment), the effective dose and safety. Proof of Concept may emerge as an optimal value gain for small pharma and the biotech industry as well as a preferred handover point to big pharma; it includes projections of commercial product viability.

The understanding of the human genome will revolutionise the discovery and development of new medicines. Genomics will fractionate human disease and thereby reduce the number of individuals for whom drugs will be tailor made. This segmentation of medical needs on one side and the very high cost of today's drug development on the other request drug research and development processes that at equal high quality are even faster and certainly cheaper than today's processes.

The identification of some one hundred thousand human genes will provide between five and ten thousand new drug targets. Hundreds of thousands of new chemical molecules from existing libraries or derived from combinatorial chemistry will be screened ***in silico*** with the help of robots.

High throughput screening systems (HTS) - ultra, smart or highly selected - will predefine in a functional genomics approach pathophysiological, toxicological, metabolic and interactive drug-drug properties as well as the influences of concomitant disease. Following lead identification and optimisation Clinical Drug Candidate selection will become a formidable decision task. This can only be resolved with new bioinformation management technology which allows to cope with the unimaginable information generated in the drug research and screening process.

This high throughput drug discovery and lead optimisation process will enable preprofiling (and selection) of a compound and better planning of clinical proof of principle testing, the pivotal phase III trial, ongoing NDA preparation and successful market introduction.

Entry into the drug development portfolio could start as early as at the clinical candidate selection point from which point onwards development could be project managed optimally.

Preclinical characterisation of new chemicals up to entry into man will greatly benefit from predictors found in functional genomics, ***in vitro*** human cell tests, from mechanism based modelling and simulation derived from animal experimentation as well as allometric scaling. At entry into man, exploratory clinical research and

indication finding on the bases of minimal toxicology testing will enable ‘economical clinical lead optimisation.’

Clinical proof of concept, in a collapsed phase I and II will be achieved by better planning and evaluation of clinical trials including simulation and modelling techniques, novel statistical adaptive design approaches as well as genome based subject selection. Proper definition of biomarkers and/or surrogate endpoints will expedite the proof of concept testing. The proof of concept can be sought with a minimum dose of satisfactory effects before the full human tolerance testing is being done; challenge or provocation tests may be of further help.

Such future ‘high throughput drug development’ also calls for a new type of a generalist drug developer (MD) who understands the management of particular diseases from genome to integrated health care as well as the commercial aspects. Here is a new role for an 'R&D Value Developer' also serving the Biotechnology Industry.

How to bring new biotech molecules into deliverable products?

Prof. Daan J.A. Crommelin, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University and OctoPlus B.V., Leiden,
The Netherlands

Protein drugs (biopharmaceuticals) have established a firm position in our present arsenal of therapeutic agents; the pipeline of biotechnology derived products to be launched in the near future is well filled. However, their therapeutic effects are still not utilised to the full extent and their administration is usually patient unfriendly as they have to be administered through injections. Unfavourable biopharmaceutical and pharmacokinetic properties of these compounds are responsible for this unsatisfactory situation. The emerging gene therapy approaches suffer from the same disadvantages.

Causes of failure of the present generation of protein drugs and gene therapeutics in fighting diseases such as cancer and certain microbial, parasitic and viral diseases can be summarised as follows:
- The active compound is rapidly eliminated (cleared) in intact form from the body through the kidneys or the liver, or inactivated through metabolic action and, therefore, it does not reach the target site in sufficient amounts.
- Accumulation of the drug at the target site is the exception and not the rule; most of the drug is distributed over other organs exerting its toxic effects there. Passage of endothelial and epithelial linings of body compartments is often not easy for these highly charged/polar and high molecular weight materials.
- Internalisation of a protein or genetic material into target cells is often rather low, which poses problems in particular if intracellular delivery is required for its action. And even if the drug enters the target cell, it is easily destroyed before reaching its cellular target site.

On the basis of the above, it is clear that targeted delivery of protein drugs and genetic material for gene therapy is highly desirable to improve the therapeutic performance of these materials. As Tomlinson expressed it: drug targeting is (only!) a question of DART: collect all possible information on the Disease, provide target site Access, and generate the desired drug/gene Retention and Timing of its presence (Tomlinson, 1987).
Therefore, protein and gene targeting approaches should pay attention to all four of the above mentioned aspects.

Present research programmes focus on improving target site accumulation by novel delivery systems; they have met with limited success so far. But, our insights into the nature of pathological conditions at the tissue and cellular level and the mechanism of action of drugs have grown enormously over the last decades and should help us to rationally design much better performing, targeted delivery systems.

If a protein or gene does not have an inherent tendency to accumulate at its desired target site (the 'normal' situation), a common approach to achieve successful, site specific activity is to utilise a homing device-carrier combination. The homing device is responsible for site specific accumulation, the carrier (a small vesicle or macromolecule) for metabolic protection and required pharmacokinetic characteristics (e.g., prolongation of blood circulation time). Many homing devices and carrier systems for targeted protein delivery have been developed over the last decade and some of them are presently being used in therapy. The strategies for ***in vivo***, targeted delivery of genes have not reached that stage yet.

A point that has received relatively little attention so far is the formulation of pharmaceutical proteins and genes in the their dosage form. Full characterisation of these large, high molecular weight molecules is necessary to ensure a constant quality and to guarantee their therapeutic performance and safety, but this goal was difficult to reach. However, huge advances in analytical methodology have made it possible to replace -at least partly- the traditional animal tests and bioassays. This trend provides opportunities to speed up the formulation programmes of biopharmaceuticals.

In conclusion, the classical 'magic bullet' concept for targeted delivery of proteins and genes is still in an early stage. Much basic and development work is needed to ensure successful targeting. Moreover, formulation programmes of biopharmaceuticals may be shortened if the full potential of modern analytical techniques would be exploited more vigorously.

Tomlinson, E. (1987). Theory and practice of site-specific drug delivery.
Adv. Drug Delivery Rev. 1: 87-198.

Appendix 2 List of participants

Workshop on New Safe Medicines Faster

Name	*Company/Institution*	*City*	*Country*
Ahr Gertrud	Bayer AG	Wuppertal	Germany
Alderborn Göran	Uppsala University	Uppsala	Sweden
Artursson Per	Uppsala University	Uppsala	Sweden
Axelsson Anders	Lund University	Lund	Sweden
Bayliss Martin	Glaxo Wellcome R&D	Greenford	UK
Bergmann Karen Ann	Novartis Pharma AG	Basel	Switzerland
Bjerrum Ole J	Novo nordisk A/S	Bagsvaerd	Denmark
Bloisi, Wilma	Zambon Group Sp.A.	Besso	Italy
Bogataj Marija	Ljubljana University	Ljubljana	Slovenia
Bogentoft Conny	Karolinska Innovation AB	Stockholm	Sweden
Bopst Martin	UCB Pharma SA	Braine l'Alleud	Belgium
Broesen Kim	Odense University	Odense	Denmark
Brokmose Pia K	Novo nordisk A/S	Bagsvaerd	Denmark
Brughera Marco	Pharmacia & Upjohn	Nerviano	Italy
Buntinx Agnes	Merck Sharpe & Dohme	Brussels	Belgium
Bühler Fritz R	ECPM Executive Office	Basel	Switzerland
Caldwell John	Imperial College	London	UK
Carrondo Manuel	IBET	Oeiras	Portugal
Clark Brian	Bradford University	Bradford	UK
Connolly Ann	SmithKline Beecham	Welwyn,Herts	UK
Crommelin D J A	Utrecht University	Utrecht	The Netherlands
de Jong Henk	I.R.I.S.	Courbevoie	France
de Leede Leo	Yamanouchi Europe BV	Leiderdorp	The Netherlands
Debressine Leon	Organon International BV	Oss	The Netherlands
Denaro Maurizio	Bracco S.p.A.	Milano	Italy
Dencker Lennart	Uppsala University	Uppsala	Sweden
Denèfle Patrice	Aventis	Vitry sur Seine	France
Devine Joan	Covance Laboratories	Harrogate	UK
Diderichsen Börge	Novo Nordisk A/S	Bagsvœrd	Denmark
Dingermann Theo	Frankfurt University	Frankfurt	Germany
Donald Stuart	CMR International	Epson	UK
Döring Gerd	Hygiene-Institut	Tübingen	Germany
Fildes Frank	AstraZeneca	Macclesfield	UK
Fischer Guenther	Hoffmann-La Roche Ltd	Basel	Switzerland
Folestad Staffan	AstraZeneca R&D	Mölndal	Sweden
Frøkjœr Sven	Royal Danish School of Pharmacy	Copenhagen	Denmark
Garzia Rafaella	Chiesi Farmaceutici S.p.A.	Parma	Italy
Gaviraghi Giovanni	Glaxo Wellcome S.p.A.	Verona	Italy

Gilbert Pierre	Eli Lilly & Co	Mont Saint Guibert	Belgium
Gottesdiener Keith M	Merck Sharp & Dohme	Rahway	USA
Graepel Peter	Pfizer Centre de Recherche	Amboise	France
Graffner Christina	Medical Products Agency	Uppsala	Sweden
Grahnén Anders	Quintiles AB	Uppsala	Sweden
Grossi Enzo	Bracco S.p.A.	Milano	Italy
Grymbowski Thomas	Gruenenthal GmbH	Aachen	Germany
Guenthert Theodor	Hoffmann-La Roche Ltd	Basel	Switzerland
Gurrieri Giovanni	Zambon Group S.p.A.	Bresso	Italy
Görög Sándor	Chemistry Works of Gedeon Richter	Budapest	Hungary
Hansen Bruno	Euorpean Commission	Brussels	Belgium
Hening Peter	Novartis Pharma AG	Basel	Switzerland
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Hincal Attila	Hacettepe University	Ankara	Turkey
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Libert Valery	Eli Lilly & Co	Mont Saint Guibert	Belgium
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Lindeke Björn	Swedish Academy of Pharmaceutical Sciences	Stockholm	Sweden
Lindén Hans H	EUFEPS Secretariat	Stockholm	Sweden
Lloyd-Smith Malcolm	Du Pont Pharmaceuticals Ltd	Stevenage	UK
Lues Inge	Merck KgaA	Darmstadt	Germany
Lund Hansen Torben	Novo Nordisk A/S	Bagsvœrd	Denmark
Luria Xavier	Almirall Prodesfarma S.A.	Barcelona	Spain
Marselos Marios	Ioannina University	Ioannina	Greece

Merten Otto-Wilhelm	Genethon III	Evry	France
Nilsson Maj-Inger	Pharmacia & Upjohn	Brussels	Belgium
Pelkonen Olavi R	Oulu University	Oulu	Finland
Penninckx W	Belgian Medicines Commission	Brussels	Belgium
Perrin Marc-Antoine	Aventis	Vitry sur Seine	France
Popp James A	Du Pont Pharmaceuticals Company	Newark	USA
Pubben M G	Merck Sharp & Dohme BV	Haarlem	The Netherlands
Rasmussen Poul	Leo Pharmaceutical Products	Ballerup	Denmark
Reden Jürgen	EFPIA	Brussels	Belgium
Renneberg Jan	Danish Medicines Agency	Brønshøj	Denmark
Rowland Malcolm	Manchester University	Manchester	UK
Ryder Hamish	Almirall Prodesfarma S.A.	Barcelona	Spain
Schnurr Erhard	Merck KgaA	Darmstadt	Germany
Selch Larsen Claus	Royal Danish School of Pharmacy	Copenhagen	Denmark
Seuter Friedel	Bayer AG	Wuppertal	Germany
Shearin Alistair	Price Waterhouse Coopers	London	UK
Shymko Ronald M	Novo Nordisk A/S	Maaløv	Denmark
Sjöström Brita	Pharmacia & Upjohn AB	Stockholm	Sweden
Sundström Michael	Pharmacia & Upjohn	Nerviano	Italy
Söndergård Thomsen	Novo Nordisk A/S	Bagsvœrd	Denmark
Tambuyzer Erik	Genzyme	Leuven	Belgium
Tasker Timothy C	SmithKline Beecham Pharmaceuticals	Harlow Essex	UK
Toffano Gino	Zambon Group S.p.A.	Bresso	Italy
Toutain Herve	Aventis	Vitry sur Seine	France
Wahlestedt Claes	Karolinska Institute	Stockholm	Sweden
Valenti Eduard	LaboratoriosDr Esteve S.A.	Barcelona	Spain
van der Waart Menno	Organon International BV	Oss	The Netherlands
Vessman Jörgen	AstraZeneca R&D	Mölndal	Sweden
White-Guay Brian	Merck Sharpe & Dohme (Europe) Inc.	Brussels	Belgium
Witte Eric	Novo Nordisk A/S	Bagsvœrd	Denmark
Vromans Herman	Organon International BV	Oss	The Netherlands
Vuorela Pia	Drug Discovery Technology Center	Helsinki	Finland
Wyatt David A	Glaxo Wellcome R&D	Greenford	UK

In addition, there was a small number of on-site registrations, including officials and civil servants of the European Commission, attending all or part of the programme.