forms part of a social budget that also contains pensions and unemployment. Given the older population and the near double average unemployment rates, the social budget is under far greater pressure in Europe compared to the USA.

In Europe, spending on health care continues to grow as a percentage of GDP, with no clear Europe-wide shift towards an increase in private sector funding. Although pharmaceuticals represent a minority of health care spending, the rate of growth of spending has exveeded that of total health care.

Pharmaceutical growth is outstripping total health care growth in almost every major European country. Spend on pharmaceuticals tends to be an easy political target. Payers are forced to adopt drastic measures to curtail cost growth even in innovative areas like cancer. How the necessary health care resources should be allocated is a source of contemporary debate.

"Spend on pharmaceuticals tends to be an easy political target. Payers are forced to curtail cost growth in innovative areas"

In pharmaceutical markets the focus of cost containment has been on primary care, and the penetration of generics has been higher in the GP-initiated segment than in the specialist-driven sector. Class cannibalisation has provided increased opportunities for generics in Europe, so there is some debate as to whether the same will be seen in the USA in 2006. An example would be that generic lisinopril is gradually taking prescription share from other ACE inhibitors.

"The penetration of generics has been higher in the GP-initiated segment of the industry"

Generic market dynamics

The cost squeeze is driving manufacturing east; by 2012, India will become the primary manufacturing source for generics and a large brand player. The country already ranks as the number four global player by volume, and accounts for 70% of API production. Forty-five per cent of drug master files at the FDA are of Indian origin, up from only 5% in 2000. India also has a focus on finished dosage forms, and on the penetration of emerging markets, notably China, Japan and Russia. Indian players are already looking further east to China to drive down costs still further.

On a global basis very low growth is expected for the top ten companies and there will be major divergencies in performance. There has been a large growth gap between generics and brands in 2005, and drug pipelines are dominated by specialist care drugs.

"On a global basis, a very low growth is expected for the top ten pharma companies"

Some further considerations

As mentioned earlier China continues to surpass world market growth as the USA slips and the UK dives, and beyond the top ten there are several strong, smaller markets. The top ten corporations have had various fortunes, and for the top ten products in 2005, global patent expiry is impacting some of them. The fastest growing products in 2005 contribute $16 billion in global growth, but for the leading five therapy classes in 2000-2005, their growth contribution is slowing down, contributing $4.7 billlion in 2005 versus $15.1 billion in 2003.

In addition, the FDA issued a record number of black boxes in 2005. The number of drugs given a black box warning has nearly doubled over the past year, and January 2005 (three months after the withdrawal of Vioxx) holds the record with the highest number of black box warnings in a single month. In 2006, the FDA has issued sweeping changes to drug labels to reduce medical errors. However, the period 1990-1999 showed the highest number of withdrawals due to serious safety concerns.

Launches of new active substances

Despite the rise in products in the R&D pipeline, the global new active substances (NAS) launches level is still well below that of ten years ago. Notable launches in 2005 included Byetta, for blood sugar control; Lunesta, for treating insomnia, and Macugen, which treats neovascular age-related macular degeneration.

In 2005, global NAS launches stand at 30, and generated sales of $575 million in 2005 in 24 countries. Ninety-five per cent of the sales were in the USA. Four new cancer treatments were launched and 16 NASs were first launched in the USA. On average NASs in 2005 took 11 years and 11 months to reach the marketplace.

New launches for 2006 expected include Gardasil, a quadrivalent vaccine against human papillomavirus (HPV) types 6, 11, 16 and 18; and Cervarix, a bivalent vaccine against HPV types 16 and 18.

Reviewing the R&D pipeline

The number of active R&D projects increased again last year. Phases I and II are growing in strength, so is this a good sign for the future. Launches for 2005 and potential launches for 2006 reflect the trend of increasing specialist products, and biotechnology projects account for 27% of the active pipeline. As much as 40% of late-stage biotechnology projects in late phase development are for cancer, whereas only 15% of late-stage non-biotech projects in late-phase development are for cancer and 20% for CNS.

Emerging trends and technologies

There is a total of 1,936 preclinical registered active biotech projects in the R&D pipeline and 290 of the projects

(15% of the total) originate and/or are licensed by the top 20 pharmaceutical corporations. Of the 87 active biotech projects in late-stage development, 33 projects originate or are licensed by the top 20 pharmaceutical corporations. Of the 102 biotech products launched since the late 1980s, 73 are marketed by the top 20 pharmaceutical corporations.

The worldwide biotechnology market has topped $51 billion and continues to grow well at 18%. Europe and the USA account for 90% of the market, but other geographies cannot be ignored. Japan's contribution to the global biotechnology market continues to slip, and the leading players in the biotech market reflect a greater concentration than in the pharmaceutical market overall. Amgen markets five of the global biotech blockbusters, and immunoglobulins and proteins are on the fast track. Many of the leading biotech therapy classes are directed towards cancer, and seven therapeutic classes contributed 86% of the $7.7 billion absolute growth.

"The worldwide biotechnology market has topped $51 billion and continues to grow well"

What's next for pharma R&D?

Diagnostics are improving the targeting of expensive treatments, which is essential in the detection of cancers. Delivery systems are set to transform the way some pharmaceuticals are administered, for example gold nanorods and needleless vaccinations are nearing reality.

"Diagnostics are improving the targeting of expensive treatments, which is essential in the detection of cancers"

Assessing the impact of India and China

The acceptance of IPR by India is seen to be a major boost for high growth expectations in the future and experience suggests that acceptance f IPR has impacted many markets positively, for example Jordan and Brazil.

India has an increasingly strong position on generics in the US market. One inevery four applications to market finished medicines in the USA is by an Indian company.

"The acceptance of IPR by India is a major boost for growth"

Indian companies are establishing a reputation as reliable low-cost manufacturers in a market with the world's highest drug prices. Indian companies are not afraid to take on major players in the USA and Western Europe, as evidenced by their legal challenges on existing patents.

India has an advantageous position and continues to expand its contract manufacturing business. The country has 71 FDA-approved plants and is already establishing leadership in bioinformatics thanks to its IT industry success.

Companies are realising that China will be a major force in global supply chain activities for manufacturing and R&D. The country is increasingly viewed as a hub for Asian supply from APIs to finished goods. In R&D, many firms are establishing centres and partnerships with local institutions to capitalise on key advantages, including cost, speed of recruitment, local use and label and good government relationships.

Proper execution and partnership is where it all comes together. The biggest single challenge in China is execution. Many companies are struggling with building a profitable and reputable industry in a complex market. China represents a market of great opportunity but there are also major challenges, requiring investment, leadership and detailed execution.

Given the 2005 performance of 20.4% annual growth, and the future forecast of 15-18%, China is the future market. Leaders are investing significantly in this area, and now is the time tomove to build a competitive advantage.

The keys to success include having a clear market positioning and a robust plan for growing core market areas. A plan for penetration beyond Tier 1 cities. Well-thought-out tactics on sales force strategy and execution, and a well-thought-out HR plan for making your people a competitive differentiator. sp²

FURTHER INFORMATION

This article is based on presentations by Graham Lewis and Carl Fearn of IMS Health made at the IMS Health Pharma Horizons Seminar presented during DCAT Week held at The Waldorf-Astoria Hotel, New York City, USA in March of this year. Further information is available from IMS Health:

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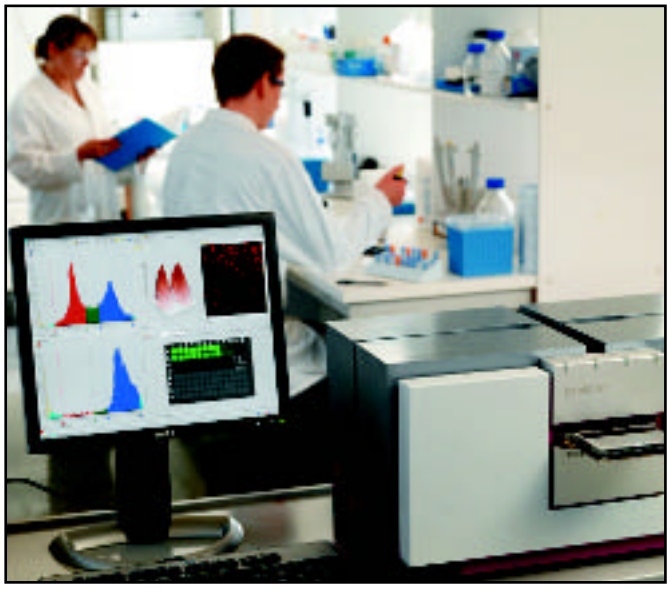
Technologies for cell-based screening applications

Fluorescence microplate cytometry for high-content screening for protein kinase activation and for cell cycle analysis are just two of the applications developed by TTP LabTech in the drug discovery assays field.

Technology company TTP LabTech's business is about forming partnerships for the application of new science to the creation of novel instrumentation and systems. The company designs, develops, manufactures and markets solutions for specific needs in the health care, pharmaceutical and biotechnology sectors. Cell-based assay development and screening is one of the company's main focus areas, and these have primarily been developed by the company's in-house biology team for use with its Acumen Explorer™ instrumentation.

A recent application for the technology has been at The National Institutes of Health (NIH) Chemical Genomics Center (NCGC) which has announced data showing the effectiveness of Acumen Explorer in high content screening at high throughput. This application of the technology was part of research being carried out as part of the NCGC's quantitative HTS (qHTS) programme.

The NCGC is at the cutting edge of small-molecule screening, running 50-70 per cent of assays in a cellular format. The work involves extensive screening of the genome and data produced can be accessed by the entire research community via a public database. The qHTS programme assays multiple concentrations of each compound and generates hundreds of thousands of concentration-effect relationships from primary screening. Consequently, there is a significant increase in wells screened over traditional single point testing, to a magnitude of 7- to 15-fold. The performance of the work required a high-throughput automated system for screening 1536 well plates.



TTP LabTech: developing fluorescence microplate cytometry for biotechnological assays.

The NCGC integrated the Acumen Explorer laser-scanning cytometer into its major screening system provided by Kalypsys, Inc. The system is being used for population distribution analysis of cells in microplates, initially providing reporter gene analysis.

The Acumen Explorer is a laser scanning rather than image acquisition system. Subsequent analysis means that data files are extremely small, which is essential in such a high-throughput system. Laser scanning and a wide field of view makes the Acumen Explorer capable of generating 300,000 data points in 24 hours working in a 1536 well format.

The fluorescence microplate cytometer enables rapid high content screening for applications such as protein kinase activation, cell cycle analysis and beta-lactamase reporter gene analysis. Its optics collect and analyse data for up to 4 colours simultaneously in a single scan across the entire well area; screening adherent, non-adherent, live or fixed cells, with typical scan and analysis times under 10 minutes a plate.

Developing a broad product portfolio

TTP LabTech, which is headquartered in the UK, is part of TTP Group. In 2003, Acumen Bioscience merged with TTP LabTech, providing a product portfolio covering screening, liquid handling and compound storage. In 2005, TTP LabTech took over White Carbon, a provider of workflow design and laboratory management software that enhances the integration of the company's products with customers' existing automation systems.

"Often, the hardest part of a partnership to create novel instrumentation and systems is translating the requirements of the core science into meaningful engineering objectives," says Wayne Bowen, product scientist at TTP LabTech. "Our scientists assist with the capture and understanding of the application and user needs, and help turn these into the functional and design requirements for the end product. Our dedicated biology and chemistry laboratories can be used to develop assays and methods, and test prototypes and production hardware under meaningful conditions."

Extending technology to cell analysis

In the late 1990s, TTP LabTech realised that its expertise in laser scanning fluorescence detection being applied to bacterial detection could be extended to the analysis of cells within microplates. The company put together a consortium of pharmaceutical companies to develop the technology into a screening instrument for high content analysis - the Acumen Explorer.

"Key design criteria were whole well analysis and plate throughputs of around 10 minutes per plate - these would ensure that the instrument was compatible with the requirements for high-throughput screening," says Bowen. "Such

results could not be achieved using microscope-based imaging technology primarily due to the limited field-of-view afforded by such optics. Thus TTP LabTech has a unique high content platform that differentiates well from the microscope-based CCD imagers and flow cytometers that perform high content analysis in the marketplace. We are continuing to enhance the capability of the Acumen Explorer, for example with more laser lines, enhanced software, and image file export, to further consolidate our position in the field of high content screening."

Further new technologies

The identification of biomarkers that can be used in the discovery of new drugs and throughout their clinical evaluation is becoming increasingly important. TTP LabTech already employs several biomarkers as screening assays on the Acumen Explorer, but is now seeking to extend their usage for development. This is being achieved by enabling the scanning of key biomarkers in tissue sections to provide their seamless use from laboratory to clinic.

"We are also concentrating on the flow cytometry market," says Bowen. "Microplate-based technologies are generally less sensitive compared to flow cytometers but offer key advantages such as an ability to analyse adherent cells in situ and greater sample throughput. Cell cycle analysis is a common flow cytometry application that we have shown to be compatible with microplate cytometry. This approach allows users to quickly identify samples of interest for subsequent analysis on lower-throughput but more sensitive flow cytometry instruments."

TTP LabTech also offers automated solutions in nanolitre pipetting and compound storage. For drug discovery, it has developed mosquito(r), a nanolitre pipettor using positive displacement micropipettes. This development enables liquid transfer down to 50 nanolitres whilst offering zero cross-contamination of samples and removing the need for unreliable, time-consuming and expensive solvent wash cycles associated with fixed-tip competitors. Its off-the-shelf applications include protein crystallography, miniaturised assays, assay ready plate preparation; and serial compound dilution. mosquito is extensively used in protein crystallography.

"TTP LabTech's comPOUND sample management system offers an affordable and scaleable method of cherry-picking microtubes from any location within a sample library with unparalleled speed and accuracy," says Bowen. "A key design criterion was to eliminate any robotic handling in the -20°C inert environment. This was achieved using pneumatics to extract and deliver compound samples within the store and to remote receivers throughout the laboratory. As more pharmaceutical organisations use smaller targeted chemical libraries for HTS to reduce costs, cherry-picking technologies such as comPOUND are a key component.

"Such innovation underlines TTP LabTech's commitment to innovation in the drug discovery process as we seek to enhance the efficiency of our clients' R&D but we are not standing still. To build on the success of our existing product portfolio, we are scheduled to launch a raft of new products for drug discovery later this year. Several will build on our significant expertise in automating synthetic chemistry processes," he adds.

Bowen says the company's business model demands that it works closely with its clients to enhance their drug discovery initiatives: "We have worked closely with Eli Lilly during their validation of the Acumen Explorer for cell cycle analysis. Software enhancements have been provided to assist the process of fully validating the instrument versus western blotting and flow cytometry techniques. In another example, we have worked with Kalypsys to validate and provide mosquito pipettors for serial dilutions in high-density 1536 well microplates.

"We are collaborating with Cell Signalling Technologies to provide a contract development service for the development of multiplex biomarker assays. This work will seek to combine CST's broad portfolio of antibodies with the multicolorimetric detection capability of the Acumen Explorer microplate cytometer," he adds.

More focused chemistry

"Drug discovery appears to heading towards screening of smaller focused subsets of compound libraries in miniaturised plate formats," says Bowen. "Whilst some of the technology exists already following the HTS revolution, significant challenges exist. Focused libraries require cherry-picking, miniaturisation required new pipetting technology, particularly in the area of compound dilution, and the increasing use of cell-based assays as primary screens demands new detection instrumentation. More focused chemistry also requires a change in chemistry workflows. At present, we are providing significant consultancy in the area of automation of synthetic chemistry to free up the time of chemists for greater challenges. TTP LabTech will address such issues as they arise with enhancements to existing products, and where required, by introducing innovative technologies," he says.

New collaborations and business prospects

"TTP LabTech will be announcing several new high profile clients for its products following a highly successful year in which all products exceeding budget," says Bowen. "Sales of our comPILER microtube reformatter doubled and we aim to repeat this success this year. With this financial year only a month old, we already have product sales of £1.5 million. A significant amount of our business is composed of repeated sales to existing clients - this is supported by reliable products and a world-class service and support team. Naturally, we also welcome new customers, so we are expanding our marketing efforts, plus will be announcing further expansions to our worldwide network of distributors. The longer term is looking promising for TTP LabTech as it continues to grow from solid commercial foundations.

"There will undoubtedly be further consolidation within the services sector," he adds. "Like drug discovery, the cost of bring new technologies to the marketplace is increasing dramatically - this can be partly offset by expanding products portfolios through merger and acquisition activity. That said, there will always be niche markets that will only be fulfilled by products from small, largely independent organisations since they are likely to be the 'blockbusters' required to support the larger product vendors. Essentially, there can be breath in terms of the technologies available but revenues will be limited," concludes Bowen. SP²

FURTHER INFORMATION

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Banishing the mysteries of evaporation and concentration

The concluding part of this two-part article by Dr Induka Abeysena and Rob Darrington of Genevac Ltd describes the latest developments in pumps, cold traps and condensers used in performing the various evaporation and concentration techniques described in Part 1.

In writing this article our aim has been to enhance the understanding of the processes of evaporation and concentration and how they work at a practical level, and through this to enable users to truly optimise their solvent removal processes. In Part 1 of the article (***sp***^{2}, April 2006, pages 48-49) we reviewed the principles and methods of evaporation and concentration.

In Part 2 we review the wide variety of hardware used in evaporation and concentration including pumps, cold traps and condensers. This article also reviews the benefits of a cold trap, the effects of pressure control and how it can be applied to speed up evaporation and prevent sample loss due to sublimation.

Vacuum pumps

Vacuum evaporation systems, such as profiled in Part 1 of this article, require a vacuum source, normally a vacuum pump. Traditional vacuum pumps have used mineral oil for the lubrication of the pump vanes. While such pumps offer good performance (eg below 0.2 mbar (0.07 Torr) with a high flow rate), the mineral oil is both messy and, over time, can be degraded by solvent vapours, causing loss of performance, and in extreme cases pump seizure.

In some laboratories, tap aspirator pumps are still used to create a vacuum. However, the high water usage of such systems and the negative environmental impact of solvent vapour condensing in and contaminating the water has led to their decreased usage.

Fig 1. An oil-free scroll pump as used in the Genevac EZ-2 Centrifugal Evaporator.

The introduction of a new generation of dry (oil-free) pumps (Fig 1) for use with evaporators and concentrators combines high performance (0.2 mbar at flow rates of 80 l/min and more) with very low maintenance and minimal environmental impact.

Cold traps and condensers

In a concentration or evaporation system a cold trap or a condenser functions as a solvent recovery system. Although it was first used to protect sensitive vane pumps from solvent attack, a well-designed cold trap can also be advantageously used to speed up the evaporation process. When solvents vaporise there is a huge volume expansion, something of the order of 20,000 times, and when the cold trap condenses vapours back to liquid, the corresponding volume reduction helps to pull a vacuum and speeds up the concentration process considerably.

Traditionally, cold traps have been made in the form of a stainless steel vessel with cooling coils attached to the outside. Typically the vessel is connected in the vapour path between the concentrator and the pump. The vessel is chilled to below 0°C by a gas compressor system, similar to that used in a refrigerator. A common problem with this design is the difficulty and time lost in emptying condensed solvent. To empty a traditional cold trap, especially when water is the solvent being condensed (as this freezes to form ice), the cold trap has to be defrosted before the trap can be emptied. To overcome this, some suppliers have introduced an interchangeable glass flask, which sits in the cold trap and collects the solvents. At the end of the concentration process the flask is exchanged for a fresh flask. However, to employ this method a thermal transfer fluid (normally silicon-based) is used to bridge the thermal gap between the stainless steel vessel and the glass flask. Changing cold flasks covered in very slippery fluid is potentially dangerous, thus the method has not proved popular.

While limited in terms of sample throughput, rotary evaporators overcome both these issues by collecting solvent as a liquid in a glass flask. The simplest glass condensers operate by chilling the outside of the glass with cooling water or dry ice.

The very latest gas compressor cold traps, such as the miVac Speed Trap shown in Fig 2, work in a similar way to a conventional Leibig condenser, in that the solvents are collected directly into a glass vessel on the front of the trap. The cooling coils are suspended directly in the vapour path and deliver up to 50 per cent more condensing power than traditional cold traps, providing higher solvent recovery. The miVac Speed Trap design also requires no cooling water or dry ice to operate and the

glass flask can be easily removed with a single quarter-turn action.

When selecting a cold trap, the condensing power is more important than low trap operating temperatures. For example, some commercial cold traps run at low temperatures eg -80°C or -104°C, but they perform inefficiently, as they consume almost all available power to reach the low temperature rather than help condense solvent vapours. Gas compressors provide cold traps with full condensing power down to about -20°C. Figure 3 illustrates the simple physical law governing any gas compressor used as a chiller. To gain optimal performance from a cold trap, it is critical to operate with full condensing power, and in the case of a gas compressor system this means controlling the boiling point of the solvents to -20°C or above. In a vacuum system this requires a pressure controller and knowledge of the solvents used.

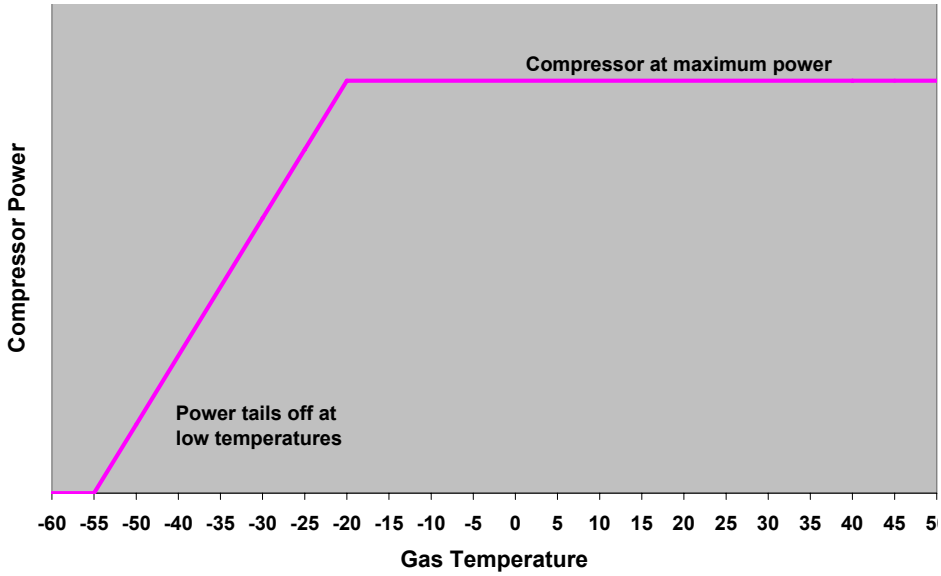

Fig 3. Cold trap power tails off at lower temperatures.

The effect of pressure control

Pressure control in a vacuum evaporation system is critical for a number of reasons: to ensure optimum trapping of evolved vapours; to speed up the evaporation of complex mixtures; and also to prevent sample loss by sublimation.

Regulating solvent boiling temperature in a vacuum concentrator is typically done by controlling the pressure (see principles of evaporation in Part I of this article). By controlling the boiling point, and thus the vacuum concentrator condensing point to -20°C, solvent is condensed at the temperature where the gas compressor cold trap has the most power, and is therefore most efficient. (It is possible to operate at higher temperatures, however this would slow down the heat energy input to the samples and the overall process. Additionally, most users prefer their samples cold, eg methanol can be efficiently boiled off and condensed at 11 mbar pressure at -20°C). Some solvents freeze at low pressures, which may be undesirable in a concentrator, therefore the pressure needs to be kept higher if this is the case. Genevac's research has found that the optimum pressure for water concentration is 8mbar, at which pressure water boils at +4°C. In the case of complex mixtures, HPLC fractions for example, where water and an organic solvent are present, the organic solvent must be removed without freezing the water, or evaporation is very slow. A specific technical note on this application is available from Genevac, see the contact details below.

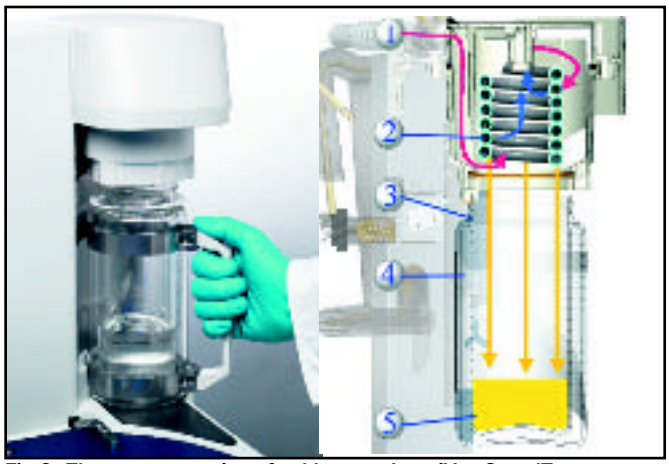

Fig 2. The new generation of cold trap - the miVac SpeedTrap. Legend: 1. Hot vapours enter. 2. Condensing coils with ice shell. 3. Glass collecting flask. 4. Vacuum insulation. 5. Solvent collects as a liquid.

Most samples can become volatile under the right conditions. Generally the smaller the size of a molecule the easier it is to volatilise, and this is especially true for organic molecules. However, when a sample is of low molecular weight (< MW 300) and/or has high volatility, for example a straight-chain organic molecule with few side-groups, then some sample may also be lost through sublimation during the evaporation process. A detailed technical paper demonstrating the importance of stopping the evaporation process as soon as the samples are dry is available from Genevac.

To summarise

The correct choice of vacuum pump and cold trap is critical to ensuring optimum evaporation and concentration performance. Pumps with appropriate vacuum level and having high flow rates are recommended. Highly efficient cold traps are available that not only speed concentration and drying rates, but that also do not freeze recovered solvents and therefore eliminate time lost during the defrosting period. For those working with samples of low molecular weight, pressure must be controlled to prevent potential sample loss due to sublimation. sp²

FURTHER INFORMATION

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APIs Europe: prospects for the generic ingredients industry

Photo courtesy of Villa Erba, Lake Como, Italy.

We present the Official Preview to APIs Europe, organised by the Chemical Pharmaceutical generic Association (CPA). The event includes the conference, exhibition, business meetings and a gala dinner, and takes place from June 21-23 at Spazio Villa Erba, Lake Como, Italy.

The APIs Europe conference and exhibition is a unique European event that joins the whole European APIs industry with its most important international customers and offers the opportunity for companies to build together future strategies. APIs Europe is the place where the best of the European APIs industry can show its latest developments to a selected number of invited international end-users.

After the success of the first edition, the Chemical Pharmaceutical generic Association (CPA) and Afaquim are organising the second edition of APIs Europe from June 21-23, 2006, at Spazio Villa Erba, Lake Como, Italy. The goal of this second APIs Europe is to further encourage and support all European APIs manufacturers to combine their efforts to maintain and expand their leading position in global regulated markets, where high quality, strict compliance to GMP and long experience with FDA inspections are a must.

The conference, 'Light & Shadows for the European API Industry: the Next Five Years', will officially open the event, and comprises three modules: International & National IP Legislation and Regulation; Markets & Qualities; Flash on Biogenerics and a Round Table in conclusion.

Special guest speakers are US Congress Representative Henry A. Waxman; Gianmartino Benzi from the European Parliament; and Renato Sicca, from the Italian Antitrust Agency.

The aim of CPA is to deliver a strong message to international markets adhering to ICH that the source of choice for high quality and the right price for APIs is still Europe, due to its long chemical tradition and to its experience in modern and regulated production of APIs.

CPA says that some people attending the last edition defined APIs Europe as 'the European DCAT'. It is CPA's intent to bring together the most important international API end-users and producers in an enjoyable and relaxing setting.

The impressive conference facilities at Spazio Villa Erba will host this year's APIs Europe event in June.

Exhibitors at APIs Europe

The following companies will be presenting their capabilities and services at the APIs Europe exhibition:

FLAMMA is a medium-size manufacturer founded in 1950 and based in the Bergamo area in northern Italy with specific expertise in the field of amino acids and related compounds. The company's expertise ranges from the production of amino acids classified as active pharmaceutical ingredients to amino acids classified as starting materials and/or key intermediates for the pharmaceutical industry. FLAMMA also operates in P.R. China with the manufacturing joint-venture Flamma Gongan Biochemicals Co Ltd for the production of some basic amino acids and with a fully-owned Research & Technology Center in Shanghai, Shanghai Flamma Bioscience Co Ltd. FLAMMA recently opened a sales and marketing office in France, Flamma SaS.

POLI INDUSTRIA CHIMICA, based in Milan, Italy, develops, produces and sells fine chemicals for the pharmaceutical industry, and manufactures a wide range of active substances using synthesis and fermentation technology in its FDA-approved plant. The company's production facilities were expanded over recent years and new facilities for research and R&D laboratories were built very recently. Poli is celebrating its 60th Anniversary in 2006.

SALARS SpA (Limited Company) was founded in Milan in 1932, and was the first and is presently the only manufacturer of opium derivatives in Italy, mainly narcotics. It is a small firm with a team of 25 very specialised employees in this unique field.

Procos is an independent and private company, founded in 1945, producing active ingredients and intermediates for the pharmaceutical market in the generic and custom manufacturing areas. The company's core know-how is in high-pressure technology - catalytic hydrogenations, carboxylations, and reductive aminations. Manufacturing and scale-up are performed according to full cGMP requirements and a strict programme of environmental and processes safety. A state-of-the-art facility on a 100,000 square metres area, with a total capacity of over 300 cubic metres, has been in operation since 1994. Products and services offered are active pharmaceutical ingredients, fine chemicals, chemical intermediates and custom manufacturing.

Edmond Pharma has expertise in manufacturing APIs such as Carteolol, Gliclazide, Indapamide, Midodrin, Oxymetholone, Prednicarbate, Procaterol, Stanozolol, Tenoxicam, Trimebutine,

Tulobuterol, Urapidil and others, as well as generics in finished form (mainly as tablets). Edmond Pharma recently expanded its chemical plant, which is approved by the FDA and by EU authorities. The company's main goal is to meet worldwide demand for its original patented chemical entity (Erdosteine) and to support the development of new APIs (such as Ropivacaine).

SIMS Srl's activities in APIs manufacturing go back to its foundation in 1937. The company, which has undergone FDA inspections since 1972, with over 20 DMFs registered at the Agency, can offer a variety of APIs with DMF along with the relevant CEP. SIMS now has a staff of 170 people and a new, state-of-the-art finishing plant has been opened at its premises near Florence, Italy, ensuring full compliance with the latest cGMP requirements.

Farmabios is a European privately owned company, founded in 1967, dedicated to the process development and synthesis of active pharmaceutical ingredients (APIs), the main classes being steroids, and antibiotic cephalosporines, and recently the portfolio has been expanded to include highly potent drugs. About 40 years' experience, productive flexibility and efficiency linked to a strong technical research background, development and innovation, have given the company the reputation of being an ideal partner to provide customers with reliable solutions, the highest levels of service and cGMP quality standards.

Moehs Ibérica, SL has been producing active pharmaceutical ingredients and custom synthesis products since its foundation in 1962. Since 1995, the company has been a member of the PMC Group. For more than 40 years, Moehs has developed advanced technical expertise and experience. The success of the company is based upon certain key values: quality of products and services; guaranteed flexibility and reliability; and cost optimisation, with economic production at its three sites (Moehs Catalana, Moehs Cántabra and Coprima).

FIS - Fabbrica Italiana Sintetici SpA, a privately owned, independent company, is dedicated to the development and production of APIs, cGMP intermediates and key building blocks for the worldwide pharmaceutical industry. Its 1450 m^3 production capacity and a half-century of production experience (FDA inspected since 1964) make FIS a strong partner, offering an integrated service from R&D to full-scale production. FIS can manage a wide range of project demands with a fast-reactive approach for every customer through its strict project management.

Sifavitor SpA was founded in 1966 as a producer of active ingredients for the pharmaceutical industry. In 1989 the company became part of the Mediolast group. The company is highly focused on quality standards. Since 1977 its quality system has been approved by the FDA and in 1998 Sifavitor achieved ISO 9000 certification, now 9001:2000.

Farmhispania is a privately owned company, established in Spain, operating two multipurpose plants. Since 1970, the company has been a leading manufacturer of advanced pharmaceutical intermediates and active pharmaceutical ingredients (APIs) for the branded and generic pharmaceutical industries.

ICROM SpA was founded in 1969 with a plant located in the northeastern region of Milan. In February 1996 ICROM became a member of the French chemical group PROTEX. ICROM is dedicated to the synthesis of bulk active pharmaceutical ingredients and fine chemicals.

EVENT PROGRAMME

Tuesday, June 20, 2006

15.00-18.00	Exhibitors' and visitors' pre-registration

Wednesday, June 21, 2006

8.30	Guests welcome/Accreditation
9.00-16.00	Conference: 'Light & Shadows for the European API Industry: the Next Five Years'
16.00	Business meetings

Thursday, June 22, 2006

9.00-17.00	Business meetings
18.30	Cocktails
20.00	Gala dinner

Friday, June 23, 2006

9.00-18.00	Business meetings

EQ ESTEVE, a member of the Spanish pharmaceutical group ESTEVE, offers process development, manufacturing and marketing of APIs for the life science industry. For more than 40 years EQ has developed innovative chemical processes for the manufacture of a wide variety of APIs that are currently used commercially in the major markets of the USA, Canada, Europe and Japan.

The **Istituto Biochimico Italiano - IBI** was founded in 1919 and has been present in national and international markets for more than 80 years. IBI dedicates its efforts to developing new therapeutic applications. It is a leading supplier of high-quality injectable penicillins.

ALCHYMARS SpA was established in 1958 and therefore has a long tradition in the development and manufacture of APIs for human and veterinary use. The company's manufacturing unit consists of a multipurpose organic synthesis plant which operates under cGMP in accordance to strict regulatory requirements and in compliance with local environment regulations.

The remaining exhibitors are **AMSA ANONIMA MATERIE PRIME SINTETICHE & AFFINI SpA**, based in Milan, Italy; **Chemo Iberica SA**, based in Madrid, Spain; **Uquifa**, based in Barcelona, Spain; and **IMS**, an Italian company offering pharmaceutical powder micronisation services according to GMP. sp²

FURTHER INFORMATION

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Out of Hours Cologne

Photo copyright: Inge Decker. Photo courtesy of City of Cologne.

Cologne, a major chemical industry centre and one of the host cities for the football Word Cup this summer, has fine dining, superb bars and a wealth of attractions and entertainment on offer.

Where to eat

ALT KÖLN
Trankgasse 7
Gegenüber vom Dom
Cologne 50667
Neighbourhood: City Centre
Tel: (0221) 137 471
Open: 11.30am-1am daily
Cuisine: Austrian, German and Swiss
The 'Old Cologne' is right beside the Hauptbahnhof (main railway station) near the Kölner Dom (Cologne Cathedral). Alt Köln is a typical 'Brauhaus', with an impressive façade and a comfortable interior that makes you feel welcome. It serves the local Kölsch beer, which comes in rather small (33cl) glasses. The menu is traditional German with hearty, meaty meals like leg of pork or sausages.

ALTER WARTESAAL
Johannisstrasse 11
Innenstadt
Cologne 50668
Neighbourhood: City Centre
Tel: (0221) 9128 850
Open: Mon-Sat 6pm-1am;
Sun 10.30am-3pm
Cuisine type: Contemporary
'Alter Wartesaal' means 'old waiting-room' and, not surprisingly, it's located in the station. It serves as a club, restaurant and concert venue, offering a classy atmosphere, and great food. It's owned by TV talk-show host and chef, Alfred Biolek.

Where to drink

SCHRECKENSKAMMER
Ursulagartenstrasse 11-15
Innenstadt
Cologne 50668
Neighbourhood: City Centre
Tel: (0221) 132 581
Open: Mon-Fri 11am-1.45pm and 4.30pm-10.30pm; Sat 11am-2pm; closed Sundays and holidays
This friendly drinking establishment has the rather unusual name of 'horror chamber'. It apparently has nothing to do with the dark side of the Middle Ages, but it has been on the site since the 15th century. Have a read of the history of the building while you enjoy a Kölsch with some typical Brauhaus food.

BANKER'S
Andreaskloster 12
Innenstadt
Cologne 50667
Neighbourhood: City Centre
Tel: (0221) 134 727
Open: Mon-Fri 11.30am-11pm;
Sat-Sun closed
At Banker's you might think you were in the City of London. But don't be put off, it has a busy but friendly atmosphere and is well worth a visit. The pub is, of course, located in a banking area and does attract the financial type, but this ensures good food and good service. Happy hour is quite early here, from 5pm to 6.30pm, starting just after most of the banks close, so this is when the bar gets really lively.

FRÜH AM DOM
Am Hof 12
Cologne 50667
Neighbourhood: City Centre
Tel: (0221) 26130
Open: 8am - 12 midnight daily
Located very near the Kölner Dom and Hohe Strasse, Früh am Dom is a well-known place that attracts both tourists and locals alike. In a way, it is to Cologne what the Hofbräuhaus is to Munich, but the beer comes in the rather small glasses peculiar to Cologne. As well as the freshly-brewed Kölsch, there's a very good menu of local and national specialities. A visit to this place is highly recommended.

Where to shop

HOHE STRASSE
Hohe Strasse
Innenstadt
Cologne 50667
Neighbourhood: City Centre
Hohe Strasse runs from the Kölner Dom to the business centre of the city, and by walking along it you are tracing the footsteps of the ancient Romans. It's an excellent shopping area with many types of store, and was the first completely pedestrianised main street in Germany.

KAUFHOF
Hohe Strasse 41-53
Innenstadt
Cologne 50667
Neighbourhood: City Centre
Open: Mon-Fri 10am-8pm;
Sat 10am-4pm
Kaufhof is one of the best department stores in Cologne. Occupying five floors, the store offers you almost anything you want. The women's and men's departments are very good, and there are special sections for individual labels. There's a restaurant on the third floor, and a hairdressers and the sports department. The top floor hosts an internet café, as well as the CD and home electronics section. On Saturdays, shoppers head for the supermarket, which offers some tasty delicacies.

4711
Glockengasse 4711
Innenstadt
Cologne 50667
Neighbourhood: City Centre
Tel: (0221) 9250 450
Open: Mon-Fri 9.30am-8pm;
Sat 9.30am-4pm
The 4711 sign dominates the view in the vicinity of the main railway station (after the Cathedral of course!) and 4711 is the original eau de cologne, a trademark of the city. The 4711 shop is dedicated exclusively to the scent. In an elegant atmosphere, 4711, also known as Kölnisch Wasser, is available in bottles of all shapes and sizes, so this should give you some gift ideas.

Where to visit

KÖLNER DOM
Hauptbahnhof
Cologne 50667
Neighbourhood: City Centre
Tel: (0221) 9258 4740
Open: 6am-7.30pm daily
This classic example of Gothic architecture was declared a world heritage site in 1996. It took 632 years to build the Kölner Dom, which was the world's tallest building when completed in 1880, at 157 metres (almost 500 feet). There's a fantastic view from the top, but you need to be pretty fit to reach the top of the towers. There are guided tours at the following times: Mon-Sat 11am, 12.30pm, 2pm and 3.30pm; Sun 2pm and 3.30pm.

INSIDE COLOGNE CITY TOURS
Bismarckstrasse 70
Belgisches Viertel
Cologne 50672
Neighbourhood: Belgian Quarter
Tel: (0221) 521 977
Explore the various historical eras of Cologne, such as Roman, Middle Ages or Third Reich, or follow a particular theme, for example, the Kölsch-Bier Tour or the cemetery tour. One of the most popular tours is the traditional Kölner Highlights sightseeing tour. There's also the entertaining horror tour, with ghost stories to send shivers down your spine. Most tours start at the Stadtmuseum, Rathaus or the Heinzelmännchenbrunnen and last around 90-120 minutes, just telephone for details.

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