

EDITORIAL

Dear Readers,

A well-known marketing slogan advises us to do good things and talk about them. I'd like to modify this saying just slightly so that it reads "develop good things and talk about them". And in fact, over the course of the mid 90s we developed a system that remains unmatched even today. We gave it the name AIS, which stands for Automated Inspection System.

To be honest, the idea to develop this was basically born out of necessity, because the type of quality control instrument we were in need of for our pharmaceutical packaging simply wasn't available on the market. However, our customers were clearly demanding this. So we worked closely with a technical university in developing a customized system that we gradually modified so that it would be able to differentiate defects. Today, our AIS has become an advanced and unique high technology tool that is capable of offering our customers exactly what they need: customized and differentiable quality that meets the highest cosmetic demands. Thanks to our AIS, we were finally able to launch our TopLine products that



are specifically designed to fulfill challenging customer requirements.

Inside this edition, you'll be receiving some interesting background information on AIS, as well as TopLine, our highest quality standard tuned according to your individual needs, and I can promise you that we will continue to expand our new expertise and, as a result, continue to invest in the future of our AIS. In keeping with our pledge to develop good things and talk about them, we'll continue to keep you informed of the progress we're making.

For today, we hope you enjoy reading our latest edition. Sincerely yours

Dr. Peter Knaus
Vice President, Business Segment
Pharmaceutical Packaging

APPLICATIONS

Tailor-made solutions for the highest requirements

Rising expectations and stricter regulations are increasing the demand for top quality primary packaging for injectables as provided by Schott TopLine vials.

Quality requirements for pharmaceutical primary packaging have significantly changed during the last few years. Safety and high product integrity as well as cleanliness and particle contamination have become a primary focus of the pharmaceutical industry, among others driven by the trends in regulatory requirements for drug containers in general and an increased

particularly important with packaging for innovative bio-technological drugs that are injected to treat diseases such as cancer, HIV infections and also for toxic substances," said Elsener, "where the costs and conceivable risks to the quality of such medications cannot justify lower quality packaging solutions." However, also for less costly drugs it can pay to use high quality TopLine containers to improve the efficiency of the filling and packing operations.

A defect that causes a container to break or a filling line to stop could quickly multiply packaging costs. A

-of-the-art, inhouse developed vision systems (see article page 4), full compliance with GMP requirements for primary packaging and an efficient quality organization and continuous improvement culture (six sigma).

TopLine customized packaging solutions are tailored to the product requirements and the product environment of the customer. The benefits for the customer are a reduction or elimination of the incoming inspection, a higher yield and productivity on the filling line, a low reject rate and an assured product safety - providing for lower overall cost. The unique combination of high quality and flexibility has proven cost reduction potential: "Our high quality, customized solutions have enabled customers to reduce the volume of defective products considerably," says Elsener. "Despite the higher price of TopLine products, customers report overall cost reductions several times higher than the money they invested. Others cite a decline in the number of product-related complaints."

TopLine products are developed in close cooperation with the pharmaceutical company. For this purpose, Schott forma vitrum sets up long-term quality improvement programs with the customer. Multi-functional project teams with representatives of supplier and customer analyze the requirements, define specifications, set target goals and begin step-by-step improvements for measurable results. "It's Schott's tailor-made approach to meet your challenges of today and tomorrow."



FDA regulatory focus on glass quality issues in particular. The high quality vials that Schott forma vitrum offers under its "TopLine" product line represent solutions that effectively address these needs.

"Higher standards for safety come at a time when the industry is also seeking to meet the demand for more efficient filling and packaging processes," said Bernhard Elsener, Vice President Marketing and Sales of Business Segment Pharmaceutical Packaging at Schott. "There seems to be a conflict between cost and quality - but we at Schott can prove it is not."

Vials that are used to store highly sensitive drugs must fulfil a number of special requirements. They must be totally free of scratches, deformations or microcracks that could lead to breakage and/or leakage. At the same time, they must be completely free of even the lowest level of contamination that could possibly react with substances. "This is

cosmetic defect of a container can lead to unnecessary rejects. In the same way, impurities or difficulties while administering a medication could translate into risks for the patient. Either way, the cost is high, what is required are high quality products to ensure maximum safety: reliable packaging units that successfully withstand filling and application.

TopLine meets these standards with a line of products that rely on premium quality glass tubing and advanced forming technology, excellent process capability due to vision systems and validated processes, 100% inspection of cosmetic aspects with state



SUCCESS STORY

Interview with Chiron about TopLine vials

Consistent high quality and customized specifications with TopLine vials by SCHOTT forma vitrum

No biotech company has had a greater impact on human health worldwide than the Chiron Corporation. As a multi-dimensional company with businesses in biopharmaceuticals, vaccines and blood testing, Chiron has been at the forefront of improving lives around the globe. By developing new products, exploring new indications for existing products and expanding market reach, Chiron will continue to bring improvement to health around the globe.

Chiron uses Topline vials by SCHOTT forma vitrum. Tor Ramsland, Associate Director Supply Chain Management,

Chiron, discusses the experiences with TopLine vials from SCHOTT forma vitrum.

Since when and for what medication or drug are you using TopLine vials from SCHOTT forma vitrum?

Tor Ramsland: Chiron has used TopLine vials since June 2003 in commercial and clinical products in our Biopharmaceutical Division.

Why did you select TopLine vials?

Tor Ramsland: Chiron has a long-standing relationship with Schott forma vitrum going back many years. Previous to TopLine vials, we were working with StandardLine

Continue page 2

vials from SCHOTT forma vitrum. These vials have a high level of quality but cannot guarantee the same benefits as Topline – 100% inspection using camera system and very tight, customized specifications. This will allow us to minimize waste due to cosmetic defects and eliminate risk of rejecting lots due to critical defects.

Where do you see the benefits of TopLine vials for Chiron?

Tor Ramsland:

1. TopLine vials guarantee consistent quality due to all-criteria, 100% camera inspection for dimensional parameters and cosmetic defects.
2. We have been able to align our incoming and final product specifications with SCHOTT forma vitrum.
3. Minimized cosmetic defects and eliminated critical defects.
4. Significantly reduced time spent on vial related quality issues.
5. It is also a benefit for Chiron to work with the technology center for vials of SCHOTT forma vitrum and take advantage of their broad knowledge of vials and appropriate use.

How would you describe the process of introducing TopLine vials? What were your experiences?

Tor Ramsland: Prior to the introduction of TopLine we had several discussions with SCHOTT forma vitrum on how to meet the stringent requirements in our industry. SCHOTT forma vitrum presented TopLine as a solution and after evaluation of a number of factors (with quality being the most important), Chiron felt that TopLine is what we need to ensure consistent high quality for our end products.

After the decision was made, a joint team of Chiron and SCHOTT forma vitrum representatives was established. This included people from procurement (project lead), manufacturing, quality, quality control, validation, manufacturing sciences and other critical groups.

Several meetings were held at Chiron, personal and via conference calls, to educate Chiron on TopLine and its capability and to educate SCHOTT forma vitrum about our specific requirements. The next step was specification alignment: the



starting point was the TopLine Standard AQL/Defect Category List. The team worked together to customize these specifications to meet Chiron's

requirements and to allow us to align all the specifications. The last step was a validation/qualification shipment with four lots for production.

The timeline from start of project to consumption in our production was about eight months. We did not experience any significant issue during implementation. The only issue was normal adjusting to specifications as we gained more experience with TopLine capabilities.

What were the challenges?

Tor Ramsland: The challenge was alignment of specifications. We invested a significant amount of time discussing defect definitions, acceptable defect size, etc. The end result, however, is aligned specifications, definitions, and a common understanding of what a defect is.

Looking back at your decision, would you choose TopLine vials again?

Tor Ramsland: Yes, definitely. Quality is our number one priority. Topline vials ensure consistent quality and specification flexibility to align with specifications.

Thank you for this interview, Mr Ramsland.

MATERIALS

COC Polymer in the focus

'Plastics for Vials' article now available from Schott

For a company with no history of using plastics as a primary packaging material for parenteral products, the first project can be a voyage into the unknown. For those considering the first step, SCHOTT forma vitrum is now making available reprints of industry consult-

ity, high purity, and biocompatibility, all in a medical grade formulation. To help explain the phenomenon, Eakins provides a brief background of COCs, their properties and their growing role in medical packaging. He also touches upon historical areas of concern, outlining the implications for COCs in such areas as pharmaceutical development, manufacturing, supply, and regulatory procedures.

With more than 20 years in the industry, Eakins is a principal consultant at Eakins & Associates, which specializes in pharmaceutical packaging for parenteral products and anti-counterfeiting strategies. He was a speaker at "Pharma Symposium 2004" held by SCHOTT forma vitrum in Mainz, Germany, last October. There he spoke on trends in regulatory requirements for drug containers and how trends in the pharmaceutical industry affect the use of primary packaging materials.

For those considering plastics for the first time, Eakins suggests building a knowledge base, beginning with a reliable supplier. SCHOTT agrees: to order a copy of Eakins' article, contact Christa Fritschi at:

christa.fritschi@schott.com.

Product focus: parenteral formulations

Process focus: fill and finish, packaging, drug delivery

Who should read: formulation development, packaging development, pharmaceutical development, manufacturing, regulatory affairs and QA/QC personnel

TopPac by SCHOTT forma vitrum: pharmaceutical packaging made of plastics

In 2003 SCHOTT forma vitrum presented the first ready-to-fill syringe made of COC polymer to the European market for use in emergency cardiac care. This new glass-like container was developed for the primary pharmaceutical packaging market and complemented the SCHOTT



forma vitrum product portfolio with its well-established high-quality glass containers in an ideal way. SCHOTT TopPac encompasses a product family with a range of syringes and vials made of COC polymer.

TopPac Syringes are available in a range of sizes, from 1 ml to 50 ml, with the focus on the 1-10 ml containers. Thanks to the high degree of design flexibility of



are available for complete sets. In developing the new pharmaceutical containers, SCHOTT worked in close cooperation with the pharmaceutical industry in order to meet their needs as well as those of the patient. Concentrated knowhow has been invested in their development

Topas® COC polymer from Ticona, SCHOTT is able to offer design features such as integrated luer lock. TopPac containers are supplied ready-to-fill, i.e. after production in a clean room using injection molding technology, they are packed, sterilized and then delivered clean and sterile directly to the customer's clean room. Rubber components from major manufacturers

which took its origin at the Otto Schott Research Centre in Marienborn, Germany in the late 1990's. Today, all production takes place at SCHOTT Schweiz AG in St. Gallen, Switzerland, a company founded specifically for this purpose and which is certified according to ISO-9001:2000 and ISO 13485 (medical device). Schott TopPac prefillable syringes are manufactured according to Good Manufacturing Practice (cGMP) guidelines. They meet European, Japanese and US Pharmacopoeia standards. Drug Master File 18416.



Michael N. Eakins

ant Michael N. Eakins' primer on the subject, "New Plastics for Old Vials," a five page article which appeared in the June 2005 issue of BioProcess International magazine.

In his article, Eakins points out that until the advent of cyclic olefins (COC), pharmaceutical companies had been cautious when considering plastics as an alternative for parenteral vials, bottles or pre-filled syringes. Now they start to discover COC's overall combination of suitable properties, including its glass-like transparency, low moisture permeabil-

Masthead

SCHOTT forma vitrum
NEWSFLASH

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ON TOUR

Producing quality with passion in Mexico

From a small town in Mexico, SCHOTT produces world class quality for pharmaceutical packaging customers in North, and Central America – and the world beyond.

The climate is tropical and company gatherings typically feature salsa music with its insistent Latin beat. But the work ethic is tremen-

and sugar – but the location is well-situated for producing pharmaceutical packaging.

Ampoules and vials were the plant's products when it opened 15 years ago with one shift and 25 employees. Today, the site has grown to include 260 employees and 60 production lines for



dous and the passion shows. "The typical work week in Mexico is 48 hours – six days a week – and that's office staff, too," says Max Kaspar, Managing Director, forma vitrum de Mexico. Here nearly a third of their 260 employees energetically engage in the company's highly popular mixed-team soccer league, bringing the same enthusiasm to their sport as they do to producing off-the-chart quality – as recently verified by an independent auditor.

Established in 1990 but with a client base that goes back over 30 years, forma vitrum Mexico operates from a constantly growing facility in the small town of Amatlan, near Cordoba, in the state of Veracruz. "We're about an hour from the Gulf of Mexico," says Kaspar, "on the coastal plain." Local industry is mainly agricultural – coffee

ampoules, vials, and cartridges. Operation is continuous, 24 hours a day, seven days a week, 340 days a year, and expansion has been steady as the market has grown. A business in microcasm, forma vitrum Mexico actively participates in several markets: 44% of the production is destined for the national market, 51% for the U.S., 4% for Central America and 1% to Europe.

Acknowledged for its quality, the plant features the hallmarks of all SCHOTT facilities: clean environment, continuous process, advanced camera inspection technology and the same machines and quality systems that ensure customers of consistent SCHOTT forma vitrum quality worldwide. "This plant has developed strong partnerships with many important market players in the pharmaceutical



industry in the U.S. over the years," says Kaspar. "That alone says a lot about our quality performance." The plant undergoes some 15 to 20 quality audits a year. "We welcome them as a way to help us improve." TPM, Six Sigma and other quality programs – in cooperation with SCHOTT facilities – keep the process continuous. "Our role is to be a centre of manufacturing excellence,"

Site at a glance

SCHOTT forma vitrum Mexico

Location:
forma vitrum de Mexico, S.A. de C.V. Amatlan near Cordoba, Veracruz, Mexico

Employees:
260

Products:
Vials, ampoules, cartridges

Capacity:
800 million units

Production area:
5,800 square meters

Quality certification:
ISO 9001, ISO 14001

says Kaspar, "which is directly related to the quality of our people." In the coming year, the plant will be adding an assembly operation to produce a new cardio imaging device for SCHOTT fiber optics, another testament to the plant's passion for quality, he says.

"Our biggest advantage is our flexibility," says Kaspar, noting that Mexican customers in particular tend to require short lead times. Their biggest challenge: continuing to optimise their processes while

maintaining profitability for themselves and their customers while anticipating their ever-growing quality requirements. "Our theme is painted right there on the wall," says Kaspar, "It reads, 'Nada grande ha sido y nada grande puede ser realizado sin pasion' – 'Nothing great has ever been and nothing great can be accomplished without passion.' It's from Georg Wilhelm Friedrich Hegel (1770-1831), the German philosopher, and it is our focus."



Celebrating 15 years of excellence

forma vitrum de Mexico celebrated 15 years of operations with two events this summer. The first, held July 15, included special guests such as the Governor of the State of Veracruz, the Swiss Ambassador to Mexico and the Honorary German Consul in the State of Veracruz along with company representatives Dr. Max Raster, Vice President of SCHOTT Pharmaceutical Systems; Dr. Peter Knaus, Vice President of SCHOTT Pharmaceutical Packaging; Guillermo Rivas, President of the Board of forma vitrum de Mexico; Dr. Ottmar Ernst, Vice President of SCHOTT Fiber Optics in the U.S.; Markus Hersche, Managing Director of forma vit-

rum AG, Switzerland; and 30 co-workers with 10 or more years of service at the Mexico facility.

Later that week, employees celebrated with an outdoor banquet followed by dancing. Highlight of the festivities was a recognition ceremony honouring employees celebrating their tenth anniversary with forma vitrum along with a special award to Antonio Estevez for his twentieth year of continuous achievement in the company. A major presence in the community, SCHOTT forma vitrum de Mexico supports numerous local organizations including recreational soccer teams, a youth boxing club, area orphanages and the state technical university.

PEOPLE

Meet Tamás Fehér



For Tamás Fehér, production manager at the Lukácsháza site in Hungary, maintaining close contact with his employees is extremely important.

"We work in an industry in which safety, quality, reliability, experience and know how really matter," Fehér explains. "We simply can't afford to have poorly motivated employees or high staff fluctuation rates," he adds. Special qualification programs, substantial benefits and an attractive bonus system are all designed to strengthen an employee's commitment to the company. And the Lukácsháza plant is extremely successful. Each year, some 750 million ampoules, 120 million vials and 25 million cartridges leave the plant as high quality products that are shipped to customers in the countries of Eastern and Western Europe, but also to Israel, India, Tunisia and South

Africa, and volumes are pointing upwards.

Fehér has now been with SCHOTT forma vitrum in Hungary since 1996. Initially, he was responsible for quality management and control for nine years. In August of 2004, he took on overall responsibility for production and maintenance. A staff of 285 now manufactures products in four different areas of the facility. In addition to ampoules, vials and cartridges, there is also a production department in charge of siliconizing products.

"Currently, we're working at full capacity. In order to be able to satisfy all of our customers' future demands, we are now expanding

our capacities," he explains with great pride. For Fehér and his staff, this will call for a complete transition from a 5 day production schedule to fully continuous manufacturing seven days a week and around the clock. New plans will have to be developed with respect to working shifts, employees will have to be retrained, processes optimized and productivity increased. "At the same time, we must keep our eyes on the costs," Fehér adds.

For the man who not only studied chemistry, but also served as an officer in the Hungarian army, safety and quality assurance will always remain top priorities: "We have no intention of rushing through this

process, nor will we have to." Initially, ampoule production capacities will be expanded. Vials and cartridge manufacturing will then follow.

Tamás Fehér is a well-equilibrated individual and everyone who knows him can see how much he enjoys his work. "I have an extremely interesting job, a fantastic team and I am given ambitious objectives and the chance to achieve them," he adds.

During his free time, the father of two children enjoys spending time outside, whenever possible sitting on the seat of his Suzuki GSX 500. "For me, enjoying nature while taking a tour on my motorcycle is life at its very best," Fehér says.

QUALITY

EFQM at SCHOTT forma vitrum

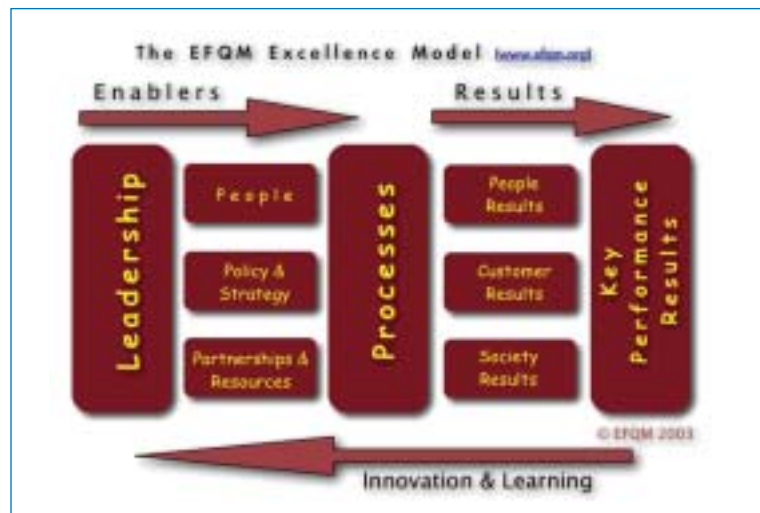
On the Way to Business Excellence. For example in Müllheim, Germany.

What traits do successful companies share? How does one become better, more efficient and more customer-oriented? These are all questions that modern companies are asking themselves today. Nevertheless, finding the correct answer is much more difficult. In 1987, Malcolm Baldrige, at that time the secretary of trade in the United States, introduced an award named after himself that was designed to encourage greater consciousness of quality that developed into a cultural trend towards more quality oriented thinking. One year later, the Europeans followed by founding the European Foundation for Quality Management, EFQM for short. Since 1992, this organization has been presenting the European Quality Award. The objective of EFQM is basically to provide those

companies that participate in Europe with a comprehensive management method with which they are able to achieve excellence or permanent high achievements at all levels of management. This refers not only to financial success, but also to identifying potential for improvement, constantly working to achieve improvements and comparing oneself with other organizations (benchmarking).

"Our goal is to become an excellent company in every respect," Norbert Reisert, head of the pharmaceutical packaging plant in Müllheim, Germany, explains. "Of course, this applies to product quality, but also to our delivery service, the perceptions of our employees and the surrounding environment and how well we manage our resources," he adds.

For the plant in Müllheim, participation in the EFQM model is just as mandatory as for all of the other



units of SCHOTT Pharmaceutical Packaging. Müllheim has already participated in the three initial levels and was reviewed by an external auditor for the first time in 2005. EFQM will also be used to assess the progress being made with regard to SCHOTT Vision 2010.

"We're still at the very beginning, however we view EFQM to be just the right assessment method for documenting whether or not we are on the right path," Reisert explains. The initial positive results that the audit yielded confirm that this is the case. In the area of lead-

ership, the organization received high praise, due to the fact that the entire site is already well structured and objectives have been adopted at all levels. However, good grades were also received in the area of cleanliness and orderliness of the working environment, something particularly important for a company that manufactures primary pharmaceutical packaging.

"We are striving to become a reliable supplier to our customers that delivers exceptionally high quality, abides by standards, such as GMP, for example, and offers long-term security and global presence as a partner," Reisert says. "Our efforts and improvements on the road to meeting these objectives must first be monitored as objectively and transparently as possible. The EFQM model is ideally suited for achieving this," Reisert concludes.

TECHNOLOGY

Searching for defects

Measurable success by total inspection with AIS Automated Inspection System by SCHOTT forma vitrum

TopLine by SCHOTT forma vitrum offers individually designed primary packaging solutions for the pharmaceutical industry. In close cooperation with the pharmaceutical company, the needs and requirements are jointly analyzed, the respective specifications are set, objectives are established and improvements are worked towards on a step by step basis. These tailor-made products are designed to substantially reduce overall cost on the customer side by optimizing incoming inspection and production performance.

Such measurable improvement is based on a combination of differ-

SCHOTT forma vitrum. These three letters stand for Automated Inspection System, a unique and highly sophisticated, inhouse developed image processing system.

The AIS was developed in cooperation with a leading Swiss university back in the mid 1990s. "Our proven expertise as a leading manufacturer of pharmaceutical packaging was integrated in AIS", says Michael J. Kling, head of the testing technology sector in St. Gallen, Switzerland. "From the very beginning, this inspection system was geared to meet the unique needs of the pharmaceutical industry. Today, the AIS is an ingenious, highly advanced defect detection system that undergoes enhancement on an ongoing basis."

AIS features several unique traits



AIS is designed to meet the unique needs of the pharmaceutical industry

ly in a position to tell whether a specific defect in a glass is a scratch or a crack," says Kling. This information is continuously collected and analyzed and serves to control the production process. Above all, it is key to achieve the top quality of our high end products (TopLine and ClearLine products).

For TopLine products, the desired parameters can be set on such an individual basis that SCHOTT forma vitrum is able to deliver tailor-made packaging solutions for specific product requirements. All TopLine vials undergo extensive, 100% AIS inspection as per customer-specific TopLine specifications. The advantage for the pharmaceutical industry lies in the process improvements for more efficient filling and packaging operations which enable a reduction of quality issues during and after the filling process.

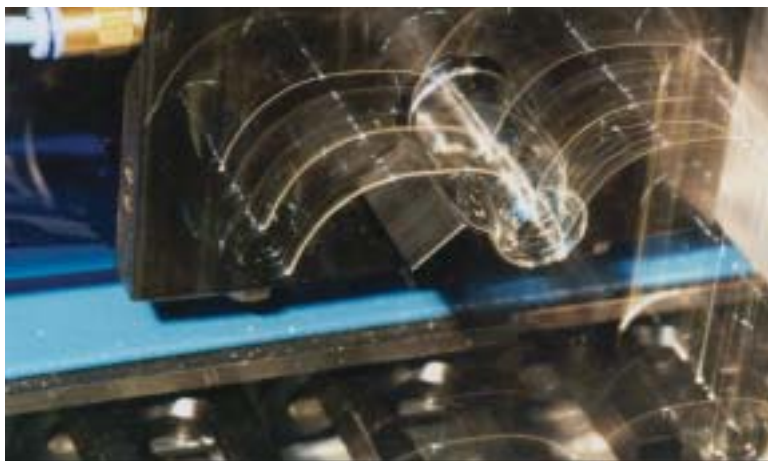
During inspection, each container is examined, from top to bottom, for cosmetic aspects and for particle contamination. 100 to 200 pic-

tures are taken of it and then compared with the tolerance values that were previously entered into the system. The system is capable of detecting even a fingerprint on the surface of glass and, given the case, sorting out this product. Defects of only a hundredth of

millimeter in size are recognized. The validation of AIS is possible, the measurable results can be reproduced. The system is fully integrated into the production process online. It provides 100% control until the end of the manufacturing

process, including product handling and transportation. The state-of-the-art vision inspection system operates in a completely automatic manner and performs without interruption around the clock.

AIS is continuously updated to ensure that the tailor-made, highly sophisticated inspection system always keeps on the highest level in terms of technology and market requirements. Currently, the AIS specialists in Switzerland are working on the development of the fourth generation of AIS. "Our goal is quite clear. We are looking to offer our customers all over the world the same validated and reproducible top quality of primary packaging. The important contribution of AIS is to enable and to ensure the same inspection standards and the same inspection process worldwide", Kling explains.



For security: reliable identification and differentiation of defects

ent, interrelated factors in a strictly controlled manufacturing process. One key factor and enabler of this achievement to be named in this context, however, is AIS by

that clearly distinguish it from conventional systems found on the market. For example, the type of defect can be classified and recorded. "Using our AIS, we are definite-

EVENTS

Exhibitions & Events

Come and see us at

- AAPS, Nashville (USA), November 6 – 10, 2005
- PDA Japan, Tokyo (Japan), November 8 – 9, 2005
- API China, Hangzhou (China), November 15 – 17, 2005
- Pharmtech, Moscow (Russia), November 28 – December 2, 2005
- Vaccine Forum, Washington D.C. (USA), January 30 – February 1, 2006
- Interphex Show, New York (USA), March 21 – 23, 2006
- Pharmaceutical Medical Packaging Copenhagen, Copenhagen (Denmark), May 9 – 10, 2006
- Interphex, Tokyo (Japan), May 17 – 19, 2006