Gerresheimer introduces metal-free syringe

Biopharmaceuticals demonstrate a series of special features. They are often highly viscous and in individual cases tend to interact with silicone oil or, for example, tungsten residue from syringe production. Gerresheimer therefore offers integrated thin-walled cannulas for the improved emptying capability of the syringe for these applications. The special silicone treatment for the reduction of free silicone oil (baked-on) and the „metal-free“ production without tungsten pin create a perfect primary packaging material for these sophisticated medications.

Metal-free syringe

A problem when using syringes can be traces of tungsten or other metals that occasionally remain behind when shaping the syringe cone in the bore. Especially for medications based on biotechnologically manufactured active ingredients, the customers therefore require pre-fillable syringes that ideally exclude the possibility of contamination with metal. With the development of an innovative production technology registered for patent, we have been able to address this wish and create a metal-free 1 ml long Luer Lock Gx RTF syringe that is ready for series production. A transfer to other Luer Lock syringe sizes or to Luer cone syringes of various sizes is possible at all times. The pin used to shape the cone with the new technology is no longer made from the tungsten usually used or an alternative metal, but instead of a special ceramic. External tests show that the new process for shaping the cone works free of residue. This means that not only traces of metal, but also contamination through the ceramics used are excluded. The Institut Fresenius neither found ceramic particles nor detected tissue reactions in a separate bio-compatibility study.

The metal-free 1 ml long Luer Lock Gx RTF syringe will be introduced by Gerresheimer at the Pharmapack trade fair on February 1 - 2, 2017 in Paris. Trade fair visitors can acquire detailed information at the Gerresheimer stand.

Baked-on siliconization for the reduction of free silicone oil

Pre-fillable syringes are very often used for the storage and administering of biotechnological medications. They are generally siliconized in order to ensure the lowest possible and most constant forces possible for the storage duration when using the syringe. The siliconization also hydrophobizes the glass surface and
Gerresheimer introduces metal-free syringe

in this way ensures the complete emptying capability for the medication and a low level of interaction of the active ingredient with the glass. However, high silicone quantities result in the formation of the smallest silicone droplets in the solution, onto which the active ingredient can coagulate and is then no longer bioavailable. With our Gx Baked-on RTF syringes patented in Europe and the USA, Gerresheimer has therefore developed a technology that achieves gap-free coating with the lowest quantities of silicone possible. In this process, a silicone oil emulsion is sprayed into the syringe body and subsequently affixed to the surface by heating. Despite the considerably reduced amount of silicone used and the correspondingly mini-mized load of free silicone droplets, the syringes provide a reliable smooth coating, as well as stable breakaway and sliding forces over the entire storage period. Gerresheimer can also equip the syringes with thin-walled cannulas that ease the administering of the often highly viscous medications thanks to their improved flow properties.

Gerresheimer AG
D 40468 Düsseldorf

Dear Readers,

We are happy to share that we kicked off February with three successful days at the LOUNGES trade fair in Stuttgart. Certainly worth a visit next year, if you are in the area. Our German readers will find a detailed report in this month’s German newsletter.

In this edition:
> LOUNGES impressions
> PAMAS Celebrates 25th Anniversary
> Pharmaceuticals Packaging: Safety across the board
> Air Flow Probe with Modbus Interface
> Hygienic Design Guarantees Cleanliness and Safety

Yours,

Reinhold Schuster

The pin used to shape the cone with the new technology is no longer made from the tungsten usually used or an alternative metal, but instead of a special ceramic.
PAMAS celebrates 25th anniversary

On June 1st 2017, PAMAS is going to celebrate its 25th anniversary. The company develops and manufactures automatic particle counters for fluid contamination control. The PAMAS product range includes measuring instruments for the cleanliness control of hydraulic or lubricating oil, water, fuel and pharmaceutical liquids. Due to their versatility, the portable particle counters of the PAMAS S40 product series are well established in various markets and applications. PAMAS will be exhibiting its particle counting instruments at the Motion, Drive & Automation show, taking place within Hanover Fair in April 2017 (Booth No. A47 in Hall 23).

Online and offline, pressureless or under high pressure, in the laboratory or in the field – the versatility of PAMAS particle counters is evident and typifies how over the years, the continued developments have ensured that PAMAS remains a world leader in liquid particle counting. PAMAS has been manufacturing automatic particle counters for fluids for a quarter of a century. With the aid of these compact and convenient instruments, the user knows within minutes if and to what extent a sample fluid is contaminated. The particle analysis technique is based on an optical measuring principle; light sensors are used to detect and count contaminants in a liquid. Over the course of the last 25 years, PAMAS has been perfecting this technique and implementing additional options and features. An example of this versatility of PAMAS particle counters is in the PAMAS S40 product series.

In addition to standard particle counting of sample bottles in a laboratory, the PAMAS S40 particle counter can also be used for online sampling. For online measurements in the field, the particle counter is integrated into a system in operation (e.g. an ongoing hydraulic or lubricating oil system). A sample of the operating fluid is extracted out of the system via a bypass valve and drawn into the particle counter. With this method, the user can verify in-situ if the sample meets or exceeds the pre-defined contamination cleanliness level.

Pressurised fluids and harsh environments do not affect the particle analysis with a PAMAS S40: Due to an integrated pressure reducer, fluids can be measured under high pressure. For particle counting in the field, PAMAS instruments are available in a rugged case that protects from harsh environment.

Practical orientation and a close cooperation with the end user turned out to be of great benefit for the development of PAMAS particle counters: Together with the end user, PAMAS began to develop individual solutions for their specific application. For an Aviation customer who wanted to analyse a corrosive hydraulic fluid, PAMAS developers built a particle counting system out of chemically stable components. The material was not affected by the corrosive sample liquid. This specific solution matured into a new PAMAS S40 product version which has been tried and tested for other applications with corrosive liquids and is available as part of our product versions.

Further product versions of the PAMAS S40 have been developed for Jetfuel and for water based hydraulic fluids that are mainly used in the Oil&Gas sector. For these applications, the particle counting results were brought into the industry-related format which is commonly used within these industries, so the user does not need any further software to convert the results. For users in the Oil&Gas sector, the particle measuring results are reported according to the SAE AS 4059 or NAS 1638 standards, and for users in Russia or China as per GOST 17216 or GJB 420.

After 25 years of research and development, the portable particle counters of the PAMAS S40 product series are now available in a multitude of adapted product versions for the cleanliness control of oil, fuel, Skydrol® and water based fluids.
“No compromising on product safety” is the overriding principle for companies of the pharmaceuticals industry and for allied enterprises in the packaging sector. Because of their high responsibility for human health, they are strictly monitored and have to observe numerous specifications and guidelines. No mean challenge for the companies concerned. From an economic point of view, this sector can still take pleasure in a market experiencing stable growth. The German pharmaceuticals market leads the field within Europe and, with annual sales of over EUR 50 billion in 2015, occupies fourth place globally. But here as well industry has to move with the times.

Pharmaceuticals packaging: safety across the board

Author: Melanie Streich, freie Journalistin

Rising life expectancy, the increase in chronic diseases and the introduction of new and often very expensive forms of treatment have been responsible for strong growth in the last few years. More and more diseases are becoming treatable. Even for rare disorders with relatively small numbers of cases, more and more medicines are being developed for which manufacturers are called upon to achieve greater complexity with ever smaller batch sizes. There is a trend away from standardisation and towards individualised treatment. For plant manufacturers and packaging system suppliers, the high flexibility and rapid retooling already demanded in the market is thus intensifying further.

For such requirements, Medipak Systems, a member of the Körber Group, offers its customers solutions that it conceives as modular, scalable platforms and gives manufacturers the necessary scope for manufacture in smaller batches and using different packages. “Our customers’ investment in production and packaging processes is immense. They require solutions that can be used for a large variety of products, can be quickly retooled and are capable of extension over their life-cycle,” explains CEO Clemens Berger.

In the future of Industry 4.0, single machines or stand-alone solutions will no longer be sufficient. Only integrated systems that take the entire value chain into account can compete in the market in the long term. The customer wants to reduce his cost per package over the entire process, and this calls for improvements in overall plant effectiveness from suppliers. Reliable plant availability is all-important here along with high machine performance and continuously high production quality.

Growth in the pharmaceuticals sector is being offset by cost reductions in the health systems in many countries with price ceilings, mandatory discounts, and benefit-based pricing or reimbursement models. There is also an increase worldwide in regulatory requirements imposed by supervisory authorities. For medicine manufacturers and packagers, this places still higher demands on the process chain as a whole.

At the same time, there is growth in the market for generic drugs, i.e. medicines whose active ingredients are identical to those of the original preparations but are sold at much lower prices. This competition encourages efficient technologies and processes to compensate for the high pressure on costs in the generic pharmaceuticals market.

Innovation in packaging design

New, innovative packaging concepts are being developed despite or precisely because of the competition from generic drugs. The introduction of the new Aspirin generation in 2014, when the Bayer Group decided to develop its classic packaging further, is an example of the most recent past. Few medicines can look back on such a long tradition - this well-known painkiller has been holding its own in the marketplace for over 115 years now. In cooperation with the Romaco Group, it has developed a new packaging technology that is adapted to consumers' changing needs. For this, the tablets are individually sealed and perforated - in the shape of a four-leafed clover. The pouches concerned consist of an aluminium/paper laminate protecting the individual tablets effectively from such external influences as light and moisture. In the design, importance has been attached to easy access - an argument that is becoming increasingly compelling in view of the growing elderly proportion of the population in the industrialised nations.

At interpack 2017 in Düsseldorf from 4 to 10 May 2017, visitors can find out about the innovative developments in the packaging sector to meet the growing demands resulting from legal provisions and consumer needs. Interesting insights into the latest production technology will also be afforded by the accompanying “components – special trade fair by interpack”. This is targeted primarily at suppliers to the packaging industry and at companies offering drive, control and sensor technology, products for industrial
Pharmaceuticals packaging: safety across the board

image processing, handling equipment, industrial software and communication, and complete automation systems for packaging machines.

**Smart packaging**

The fact that patient leaflets in a medicine package do not always have to be in printed form is illustrated by the latest further developments in packaging technology, now made possible for the first time by near-field communication (NFC). Facilitating cashless payment and keyless vehicle entry, NFC is already familiar in everyday life. Thanks to widespread smartphone use, contactless and wireless short-distance data exchange has also become of interest to the packaging sector. The possible applications range from reading-out the patient leaflet and the automatic re-ordering of drugs through to more detailed information.

Under the generic term “smart packaging”, the development of printed electronics is also rapidly advancing. Conductive plastics, inks on film, foil, paper or glass in combination with extremely thin, flexible and transparent electronic components – plus interactive displays, luminous effects and sensors – are already converging today’s packages into high-tech products. In the future, smart packages will satisfy virtually all wishes and will have to be an integrated part of an overall e-health strategy. Smart packages know the patient’s personal dosage, make the right medicine available at the right time with the aid of time-controlled access and sound an alarm when drug intake is skipped. These are innovations that are capable of improving patient safety.

**Top priority for patient safety**

Another global challenge for the sector is the problem of product piracy. The worldwide trade in counterfeit medicines is a multi-million business that causes considerable loss for the pharmaceuticals industry and, more importantly, puts the health of numerous people at risk. A joint goal of the packaging and pharmaceuticals industry must therefore be to prevent the distribution of counterfeit medicines.

Stricter guidelines and better product identification are essential for the protection of the patient. In many countries, these are already being implemented or are on the brink of being so. An example is the Commission Delegated Regulation (EU) 2016/161 of the European Union with binding provisions against the entry of falsified medicines into the legal supply chain. It states that all prescription medicines must be provided with unique identifiers and an anti-tampering device.

Specifically, this arrangement means that the medicines concerned must be marked from February 2019 with an individual serial number and be clearly undamaged – a challenge that pharmaceuticals companies and packaging manufacturers took up years ago. Uhlmann-Pac-Systeme GmbH & Co. KG has been concerned with the complex issue of serialisation since 2005 and, in the face of these challenges, has evolved into a supplier of complete solutions. Updates, new software versions and the associated advice are integral elements of today’s business. “The fact that serialisation has an impact on many processes throughout the company should not be underestimated. This is where project leaders have to drive genuine change management,” explains Kathrin Günther, responsible for the sale of software and automation solutions at Uhlmann.

Many manufacturers are resorting not only to identification, but also to the continuous traceability of their products with the aid of integrated track & trace solutions. In this area, the company offers a variety of print technologies and the possibility of label application, intelligent inspection systems, and printing and marking solutions. Depending on requirements, the components can be combined and even integrated in machines and plant in operation.

In terms of piracy-proof features, the solutions of plant manufacturers are varied. Holograms, synthetic DNA and laser codes, and special printing inks are in some cases undetectable with the naked eye. The tamper-proof seal – also known as the tamper evidence label – can be attached to the medicine package or bonded on after product filling.

Rondo, a company of the Medipak Systems Group, does entirely without safety labels and adhesives. During the closure process, punch-outs on the base and lid flaps are activated to clearly and irreversibly indicate opening. The consumer can thus see at first glance whether the package has already been opened. The pack is opened and closed just as simply and trouble-free as a conventional folded box. Another advantage is that the blanks can be processed without restrictions on existing packaging lines.

By the end of 2018, it is expected that over 75 per cent of all prescription drugs worldwide will be protected by laws of this kind and their implementation will thus become crucial for the entire supply chain.

In addition to patient and product safety, the new pharmaceuticals packages also improve the situation for the pharmaceuticals companies themselves. This is because the unique identifiability of a single medicine can considerably reduce the workload incurred by return deliveries and recalls.

**Emotional appeal at the POS**

Pharmaceuticals packages have to perform numerous tasks. They have to not only meet the complex needs and constraints of technology and safety, but also win through at the point of sale against a host of competing products. This applies particularly to over-the-counter medicines, although the competitive pressure among prescription drugs has risen significantly due to the increase in generics. Design and brand presentation make the difference here. Much like other consumer packages, the medicine
Pharmaceuticals packaging: safety across the board

Package must also appeal directly to consumers, stimulate their emotions and precisely meet their needs. For brand recognition, package suppliers use consistent designs that present all the products of a manufacturer as a uniform block on the product shelf and thus stand out from the various competition items. The purchaser's attention is held by plain language, unambiguous navigation with the aid of the design, and text arrangements without off-putting pharmaceutical jargon.

In the last few years, the drugs packaging industry has successfully accepted the various challenges in the pharmaceuticals sector and devised suitable strategies for this highly specialised business. Thanks to its huge capacity for innovation, the supply industry to the former “pharmacy of the world” is also well equipped for the future.

04th - 10th May 2017: interpack, Duesseldorf (D)

Messe Düsseldorf GmbH
D 40001 Düsseldorf

The EE671 probe is dedicated for reliable air flow measurement in heating and ventilation systems. It features the new E+E VTQ thin-film flow sensing element. Due to innovative transfer molding, the sensing element is very robust and highly insensitive to contamination, which allows accurate and long-term stable measurements even under harsh conditions.

The probe is available with fixed cable or M12 connector. The alignment strip and the matching mounting flange allow for easy installation and precise positioning of the EE671 in the ventilation duct. The sensing head design is optimized for low angle dependency.

In addition to the Modbus version, the EE671 is also available with voltage output 0-1 V, 0-5 V or 0-10 V. An optional configuration kit makes it easy to scale the output, set the Modbus parameters and perform the adjustment of EE671.

Easy integration into modern building automation systems

Air Flow Probe with Modbus Interface

The EE671 compact air flow probe from E+E Elektronik measures air velocity up to 20 m/s (4000 ft/m) and is ideal for HVAC applications. The new version with Modbus RTU interface facilitates the EE761 integration into modern building automation systems.

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Medical Seminar von ENGEL in Bangkok

Cutting-edge technologies offering a competitive advantage in the medical technology sector

With 50 participants, the medical technology seminar to which ENGEL had invited its guests at the Plastics Institute of Thailand in Bangkok in mid-December was a huge success. Together with its partner companies Fostag and Hekuma, the manufacturer of injection moulding machines used numerous practical examples to give an insight into the challenges and opportunities of injection moulding processing in cleanroom environments, while at the same time also introducing innovative concepts for machines and processing technologies.

“The development of the medical technology and health care sectors in Thailand has been quite a dynamic one”, reports Aram Tongurai, Managing Director of the Bangkok-based company ENGEL Machinery (Thailand). „This trend was in clear evidence throughout the whole event.” The participants came from established companies within the industry including international companies, as well as from smaller local firms making their first moves to gain a foothold in the medical technology market. According to Aram Tongurai, there are above all two reasons for the growing interest in this industry: On the one hand, these companies are aiming for a greater degree of independence from the automotive industry, which is quite dominant in Thailand, while on the other the quality of medical care in South East Asia is steadily on the rise, in its turn leading to an increase in production volumes and shifting the focus towards state-of-the-art solutions for manufacturing processes.

From consumables to functional components

In spite of the heterogeneous knowledge base overall, all participants were able to benefit from the presentations and the components exhibition to equal degrees. Among the most sophisticated applications introduced by Gerhard Geierlehner, Sales Engineer at the Business Unit Medical of the company ENGEL, was the highly automated multi-component production of drip chambers with integrated filters on a tie-bar-less Engel e-victory combi injection moulding machine, as well as the high-speed production of single-component interdental brushes with up to 500 bristles on an all-electric ENGEL e-motion machine. Another topic covered at the event was the cost optimisation of the mass production of components for diagnostics, such as Petri dishes, as well as highly efficient multi-component processes, which are implemented, among others, in the production of toothbrushes.

All these examples showed that high-quality equipment and custom-tailored solutions are the key for achieving optimum efficiency and minimising costs per unit, while at the same time achieving high quality and a maximum of process reliability. „Especially new entrants in the medical technology sector are looking for partners capable of delivering turnkey solutions from a single source, thereby guaranteeing a high degree of overall efficiency and safety,” explains Geierlehner. „And ENGEL is perceived as a technology leader in Thailand. It is precisely the fact that our business units have a 100 % focus on one area of application that has become a strong trust factor for manufacturers, especially in the medical technology sector.” The company even operates its own clean room at its headquarters in Schwertberg, Austria, the facility being dedicated to the development of new concepts for machines as well as to the carrying out of trials in collaboration with its customers.

Clean-room safety from a single source

From its production sites in Austria, China and Korea, ENGEL provides its customers with standalone injection moulding machines as well as highly integrated, tailor-made manufacturing solutions. Apart from the injection moulding machine itself, the turn-key production cells furthermore comprise self-developed and self-produced robots as well as individualised automation solutions, process technologies, moulds, additional peripherals as well as products which support the manufacturers' efforts of meeting the challenges presented by an age of increased digitisation and networking. The topic of Industry 4.0 is gaining in importance in Asia as well, so Gerhard Geierlehner, in his presentation, also took the opportunity to talk about the new opportunities created in this field. With its inject 4.0 program, ENGEL is keeping abreast of the trend by offering a large number of ready-to-market products for all areas of the smart factory environment already today.

In this respect, the high degree of acceptance ENGEL is gaining for its ability to provide systems solutions in Asia was once more documented by the fact that some participants started discussing specific project proposals with the experts from ENGEL, Fostag and Hekuma while the event was still in progress.

ENGEL AUSTRIA GmbH
A 4311 Schwertberg
Gerresheimer will have a range of new products and solutions for safe, reliable and convenient pharmaceutical drug packaging and delivery on show at the 20th Pharmapack. A Gerresheimer product expert will also be making a presentation on the production of multilayer plastic containers in an injection blow moulding process for the reliable protection of content against water vapor and oxygen exposure.

**Pharmapack 2017: New tungsten-free syringes, multi-layer plastic containers and excellent quality vials**

The tungsten-free 1 ml long Luerlock Gx RTF syringe premieres at Pharmapack

A problem when using syringes can be traces of tungsten or other metals that occasionally remain behind when shaping the syringe cone in the bore. Especially for the packaging of biotechnological or ophthalmological medications, pre-fillable syringes that exclude the possibility of contamination with metal are therefore called for on the market. With the development of an innovative production technology registered for patent, we have been able to address this wish and create a metal-free 1 ml-long Luer Lock Gx RTF syringe that is ready for series production. A transfer to other Luer Lock syringe sizes or to Luer cone syringes of various sizes is possible at all times. The pin used to shape the cone with the new technology is no longer made from the tungsten usually used or an alternative metal, but instead of a special ceramic. External tests show that the new process for shaping the cone works free of residue. This means that not only traces of metal, but also contamination through the ceramics used are excluded. The Institut Fresenius neither found ceramic particles nor detected tissue reactions in a separate biocompatibility study.

**Duma Twist-Off Protect**

Tommy Persson’s presentation on February 1 at 11:30 a.m. about “High-quality Primary Packaging Innovations: Multilayer Containers for Solid Dose Medications, Duma Twist-Off Protect and Senior-Friendly Closures” will provide interesting insights into the product development process.

Gerresheimer Plastic Packaging is the first company in the world to manufacture a multilayer product in an injection moulding process. Duma Twist-Off Protect and the US standard Triveni container have a multilayer design offering improved protection against water vapor and oxygen exposure. The multilayer container is also fully compatible with all existing product ranges, so there is no need for modifications to the filling line.

**Strategy to improve vial quality**

Glass vials are the most frequently used packaging for injectables in the world. Gerresheimer manufactures them in the Americas, Asia and Europe with filling volumes of between 1 and 50 ml. It recently launched an investment program spanning several years to install state-of-the-art converting machines for vial manufacturing at all its plants. The latest-generation machines and the resulting global high standards will enable it to meet even more stringent future requirements of vial quality. The new machines have now been installed at all the American plants. In Boleslawiec, where one of Gerresheimer’s two European Excellence Centers for vial production in Europe is located, the first two machines have also now been installed and put into operation. Additional new machines will be installed there in 2017 and 2018.
Its special hygienic design makes the both compact and mobile TROLLEY MAXI workstation an ideal, easy-to-clean item of equipment for demanding production environments and cleanrooms. Offering plenty of room for storage, it is the perfect complete system for use in confined spaces.

TROLLEY MAXI workstation: Hygienic design guarantees cleanliness and safety

There is no need to have a separate desk or cabinet in the same room. An integrated ready-to-connect connector plate on the back facilitates the installation of peripherals. The stainless steel casing of the TROLLEY MAXI with protection class IP65 satisfies GMP requirements. Here are just some examples of the special hygienic design features of the workstation.

**Slight inclination of the top surface**

The top surface slopes forwards slightly to prevent items being set down on it. Liquids also drain off quickly.

**Hinges and double seals**

The hinges inside the sealing area permit easy cleaning. The highly resistant silicone seals leave no gap whatsoever and can be clearly identified by their blue coloring. The clip-in sealing frame is easy to replace.

**Special fasteners**

The stainless steel fasteners are pre-assembled on the TROLLEY system and are provided with a special seal. The material and shape are designed for simple cleaning.

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Systec & Solutions GmbH
Emmy-Noether-Straße 17
D 76131 Karlsruhe
Telefon: +49 721 6634 400
Telefax: +49 721 6634 444
E-Mail: talk@systec-solutions.com
Internet: http://www.systec-solutions.com

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**Impressum:**
cleanroom online / W.A. Schuster GmbH · Mozartstrasse 45 · D 70180 Stuttgart · Tel. +49 711 9 64 03 50 · Fax +49 711 9 64 03 66
info@reinraum.de · www.cleanroom-online.de · GF Dipl.-Designer Reinhold Schuster · Stgt, HRB 14111 · VAT DE 147811997

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