Dr. Kade opts for MediSeal’s containment solution
Editorial

Dr. Kade opts for MediSeal’s containment solution

Pharmaceutical companies have in development a number of drugs with highly potent molecules which require higher safety standards during the packaging process. There is a demand for containment solutions for high potent drugs which protect the operator. The example of the Dr. Kade company clearly shows how safety standards and equipment efficiency can be achieved through customised system design.

With an eye on the cost-conscious markets of Western and Central Europe, as well as the enormous potential in the East extending as far as Russia, Rondo has greatly expanded its plant in Ejpovice in the Czech Republic. The production area has been expanded to 8000 m² and the production volume has been increased threefold. This means that standard folding boxes can be produced on this site in large quantities and Rondo quality.

For the first time, Seidenader is integrating leak detection using high-voltage technology into a fully automated syringe inspection machine. The result is an inspection machine which combines optical inspection for particles and cosmetic defects with HV inspection of integrity of the syringes. Such integration offers enormous advantages in terms of initial outlay, reduced handling and maintenance, a smaller footprint, and a reduced training requirement for personnel.

Dividella supports its customers when the TCO (Total Cost of Ownership) is calculated; this is deciding in the context of an investment decision. Against the background of changing market requirements, anticipation of future developments is playing an increasing role with a view to ensuring the essential room for manoeuvre in the future. Production facilities which respond appropriately are better prepared for changes, they can hedge their investments and are more competitive in the long term.

53 new drugs in Europe, 39 in the United States: approvals by the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) in 2012 clearly show that the pharma industry’s spirit of innovation is as strong as ever. Since 1996, the American Drug Administration has never granted as many new approvals in any one year as it did last year. In addition to drugs for the treatment of common diseases, the new approvals also concern so-called “orphan drugs” for rare diseases. More product developments are in the pipeline. On the other hand, the generics market is booming, in particular due to growing demand in the emerging economies. Diversification therefore plays a crucial role in business success – along with process flexibility. This means that special medicines, small lot sizes and high variance have to be efficiently packaged and that the volume business has to be managed successfully and cost-effectively.

55 new drugs in Europe, 39 in the United States: approvals by the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) in 2012 clearly show that the pharma industry’s spirit of innovation is as strong as ever. Since 1996, the American Drug Administration has never granted as many new approvals in any one year as it did last year. In addition to drugs for the treatment of common diseases, the new approvals also concern so-called “orphan drugs” for rare diseases. More product developments are in the pipeline. On the other hand, the generics market is booming, in particular due to growing demand in the emerging economies. Diversification therefore plays a crucial role in business success – along with process flexibility. This means that special medicines, small lot sizes and high variance have to be efficiently packaged and that the volume business has to be managed successfully and cost-effectively.

Dear Customers,

With an eye on the cost-conscious markets of Western and Central Europe, as well as the enormous potential in the East extending as far as Russia, Rondo has greatly expanded its plant in Ejpovice in the Czech Republic. The production area has been expanded to 8000 m² and the production volume has been increased threefold. This means that standard folding boxes can be produced on this site in large quantities and Rondo quality.

For the first time, Seidenader is integrating leak detection using high-voltage technology into a fully automated syringe inspection machine. The result is an inspection machine which combines optical inspection for particles and cosmetic defects with HV inspection of integrity of the syringes. Such integration offers enormous advantages in terms of initial outlay, reduced handling and maintenance, a smaller footprint, and a reduced training requirement for personnel.

Dividella supports its customers when the TCO (Total Cost of Ownership) is calculated; this is deciding in the context of an investment decision. Against the background of changing market requirements, anticipation of future developments is playing an increasing role with a view to ensuring the essential room for manoeuvre in the future. Production facilities which respond appropriately are better prepared for changes, they can hedge their investments and are more competitive in the long term.

I hope you enjoy reading this issue!

My very best wishes,

Gerhard Breu
With investments of this type, equipment efficiency, along with the overriding concern for safety, is a decisive criterion. Good accessibility via glove ports is also a prerequisite for fast and smooth change-overs and efficient cleaning. In 2012 Dr. Kade opted for a solution from MediSeal for use in production at the Constance plant.

“The fundamental decision in favour of a containment solution,” says Dr. Kade’s production manager Christian Franke, “is based on the statutory provisions.” EU Directive 89/391 is quite clear in this regard: “Collective protection measures have priority over personal measures.” In containment, however, Franke also sees benefits of a technical and economic nature: “The risk of cross contamination is considerably reduced.”

Dr. Kade opts for MediSeal’s containment solution

The Berlin-based pharmaceutical company Dr. Kade produces high quality medicines in the areas of gynaecology, proctology and pain relief/rheumatism. With more than 125 years of history, the pharmaceuticals manufacturer, with some 400 employees, achieves a turnover of approximately 80 million euros.

Its core market is Germany, with a share of about 75 percent. Dr. Kade is one of the leading suppliers of medicines in the women’s health segment of the market. These include hormonal preparations, all produced at the Constance site under containment conditions.

The best protection for employees

Classic clean-room solutions as a structural measure have significant disadvantages in terms of efficiency and operation. Pharmaceutical companies are therefore looking for alternatives with better operating conditions but equally stringent barrier effects, in order to protect employees and the environment during processing of high-potency active ingredients, by means of special safety precautions.

In this context, the isolator solution has emerged in recent years as the method of choice. It is considered in pharmaceutical production to be the state of the art. These containment solutions, which ensure a high level of protection for employees, are also in demand for solid products.

The decision in favour of the MediSeal containment solution was the right one at all times.

Needs of customers are paramount

The decision in favour of the MediSeal containment solution is justified by Christian Franke in this way: “A high degree of flexibility, a continuous focus on the specific needs of our company and the production of a persuasive project plan and an attractive range of services convinced us.” Customer focus was also fundamental for MediSeal. After an analysis of the specifications, the system specification was drawn up: machine performance, format ranges and essential functions of the line.

Parameters such as the space situation at Dr. Kade resulted in a customised system design which ensures optimal accessibility of the machine. The starting point was the CP200 thermoforming machine, in this case configured as a combined machine with roller and platen sealing. For reasons of space, it was combined with a P600 cartoning machine of extra-short construction.

One key basic requirement was the achievement of maximum functionality in the area of the isolator. A mock-up study therefore followed on from the design stage: the isolator with all its ports and airlocks (Rapid Transfer Ports – RTP) was built as a 1:1 scale model. Operators were able to test in advance all the important movement, such as the input and output on the isolator. Employee acceptance of the new line was therefore ensured in advance.

Interested? See the containment solution “live” and more at the Constance site on October 16, 2013.

For your personal invitation and further information please contact

nadine.noske@mediseal.de

Christian Franke
Dr. Kade’s production manager

“Both the decision in favour of MediSeal’s containment solution and the corresponding team were the right one at all times.”

The safety standards required by law as well as line efficiency can be ensured by a customised system design.
MediSeal

An automatic wash-in-place function with fixed cleaning nozzles was able to be dispensed with in the case of the Dr. Kade solution. Instead, there is manual wet cleaning with a hand shower. This required reconfiguration of the entire product feed area for the wet cleaning system.

Each product change is now initiated with manual wet cleaning in the containment. This binds dust from the product and the containment can then be opened safely. This allows additional classic, manual cleaning.

The product is fed in in 10-15 kg bags via a double door airlock with interlocked doors. There was therefore no need for a docking system for large containers.

Convincing results

Before implementation, Dr. Kade and MediSeal conducted a risk assessment, applying the failure mode and effect analysis (FMEA) method. According to all those involved, the considerable accompanying planning effort contributed substantially to the efficient and successful completion of the project.

The overall result is convincing: measurements of the inhalable dust on the operator for more than seven hours in each case revealed active ingredient concentrations below the detection limit.

Seidenader

A challenging development in automatic syringe inspection

For the first time, Seidenader is integrating leak detection using high-voltage technology into an automatic syringe inspection machine.

In addition to camera-based inspection of parenterals, in recent years Seidenader has been focusing increasingly on complementary inspection technologies, including the use of high-voltage (HV), polarimetric inspection or near-infrared spectroscopy to check for leaks and integrity of containers, to identify the product or to avoid cross contamination. These technologies are provided either on their own platform as a standalone machine, or integrated as a module into a Seidenader VI or MS series high-performance inspection machine.

Such integration offers enormous advantages in terms of initial costs, easier handling and maintenance, smaller footprint and reduced training requirements for operators. Beyond that all inspection results come from a single source.

The combination of multiple inspection technologies in a single automatic machine, however, also presents the development team with some challenges, as will be shown by the example of the first syringe inspection machine with integrated HV leak detection.
Inspection using HV technology

Essentially, the inspection station consists of an HV needle electrode and a ground electrode, between which an AC voltage is applied. The current in the HV circuit is measured continuously by a measuring bridge integrated into this circuit. A product which travels into the inspection station becomes a part of this circuit, mainly due to capacitive coupling.

In the case of an intact product, the voltage measured at the measuring bridge will increase up to a specific “normal value”, because the product lowers the electrical resistance in the HV circuit. This normal value depends on the one hand on the setup parameters of the HV station, which are in turn matched to the product to be inspected (format, fill level and conductivity of the liquid), and on the other hand by the ambient conditions (temperature, humidity).

If the product is not intact, a plasma is formed in the area of the defect, because of the increased electrical field strengths between the HV needle electrode and the product. A spark discharge occurs. This further reduces the resistance in the HV circuit. As a result, the current increases and the voltage across the measuring bridge is above the normal value. If a defined limit (normal value plus tolerance), establishing the boundary between satisfactory and defective syringes is exceeded, the product is classified as defective and consequently rejected as a defective product.

Two inspection carousels

In order to ensure optimal conditions for both camera-based inspection and HV inspection, the MS-S series machine has two carousels which are linked by a turn-over starwheel.

For the visual inspection, the syringes are transported vertically in the carousel with finger grip down. Doing so, particles hidden in the syringe cone are brought into motion and become detectable for the camera.

In the HV inspection station, however, presentation of the syringes in needle-down position is preferable, as in this orientation the complete surface of the inner wall of the syringe can be wetted by rotation. This is especially important for the syringe cone which is the most critical part for leak detection, thereby creating conditions for optimal HV inspection.

Nonconductive handling system

To prevent accidental flashovers, discharges, electrical leakage or interference fields at the HV inspection station, the product grippers which retain the syringe by the finger grip must be electrically nonconductive. In addition, appropriate insulation paths must be established between the HV electrodes and the electrically conductive parts of the machine. In both cases, and after many tests, a special plastic is being used. This material is extremely durable and has appropriate insulating properties in order to prevent any influence on the results of the HV measurement.

These structural modifications led to the construction of a syringe inspection machine on a MS-S platform which combines visual inspection for particles and cosmetic defects with HV inspection for integrity of syringes, with a throughput of up to 24,000 products per hour.

The HV inspection module is designed for a capacity of 36,000 syringes per hour and is also available for integration into a VI-S.
Divellla

TCO – High Flexibility

The early integration of TCO calculations in line with an investment decision assures – together with a flexible packaging and machine design – long term asset protection.

TCO calculations in the light of changing overall conditions

The production of packaging for the pharmaceutical industry is a complex process. Stringent safety requirements are combined with growing requirements for patient convenience, durability, environmental compatibility and compliance. In addition, the increasing segmentation of the market makes sophisticated secondary packaging more and more relevant. With the aim of achieving the shortest possible time-to-market, companies must also be able to manufacture new products on existing packaging machines. But the rising cost pressures in the industry mean that investment decisions are often taken on the basis of arguments based on price.

The TCO calculation (TCO = Total Cost of Ownership), by contrast, is based on the calculation of all the costs of an investment, including operating costs. TCO calculations therefore provide a good analytical basis for investment decisions. In this context, it is important to recognize any cost drivers and any hidden costs which may occur and to quantify them, as far as possible. The TCO calculation has its origins in the IT industry.

Cost components in the TCO calculation

As part of the TCO calculation, the investment costs are examined. In this context, the following cost components are essentially of relevance:

- Installation and commissioning costs
- Costs for employee qualification
- Training costs
- Costs of tools, “first aid” spare parts, etc.
- Costs for adjustments to the infrastructure and for the introduction of the machine

Operating costs are another element of the TCO calculation. Above all, in this context, the following cost components are considered:

- Personnel costs (operator costs)
- Infrastructure costs (space requirements)
- Costs for packaging materials
- Logistics costs (in the particular case of products which have to be transported in the cold chain, the volume of the packaging is of great importance)
- Energy costs
- Maintenance costs
- Overall Equipment Effectiveness (OEE)
Changing general conditions and their impact on the TCO calculation

In today’s pharma environment, for example, market trends, such as simpler forms of administration, improved compliance or environmental aspects, e.g., reduction of waste or avoidance of plastics, are placing completely new demands on the packaging solution. In addition, amended regulations, such as the addition of a pack insert or its larger size, involve necessary adjustments.

Ideally, such changes to production goals can be accommodated without major investment in machinery. It is therefore worthwhile taking this aspect into account in the decision and taking appropriate precautions at the time the investment is made. For example, space can deliberately be kept free on the packaging machine for additional future functionality. This approach allows a certain degree of investment security (or “asset protection”).

Adaptable packaging concepts and machines

In the life cycle of a pharmaceutical product, it is not uncommon for the method of administration to change: for example, the administration of the product may change from a syringe to an auto-injector. What does this mean for the TCO calculation? If a flexible packaging concept and a modular machine were purchased on the basis of a TCO calculation, this increases the chances that the machine can be converted and can continue to be used.

Conclusion

A comprehensive TCO analysis, in particular with regard to cost drivers, makes a lot of sense in the context of an investment decision. With an eye on the future, an attempt must also be made to anticipate future requirements. Changing conditions can quickly overtake original TCO calculations. In this context, flexible packaging and modular machine design help to ensure the necessary room for manoeuvre for the future. Production facilities which respond appropriately are better prepared for changes; they can hedge their investments and are more competitive in the long term.

Christoph Hammer
Chief Technical Officer/Deputy Managing Director
Dividella AG, Grabs, Switzerland

Further information and case study including example calculation see
Rondo obaly was founded in 2006, with a view to servicing the cost-conscious markets of Western and Central Europe, as well as exploiting the enormous potential in the East. Now its plant has been expanded to 8000 m² and an investment in a new, high-performance production line was made.

The Rondo AG companies are among the leading European manufacturers of folding boxes for the pharmaceutical industry. Rondo obaly in Ejpovice in the Czech Republic is a fully-owned subsidiary of Rondo AG, based in Allschwil, Switzerland. In Switzerland, it is mainly so-called “special products” which are produced, i.e. folding boxes for special products and applications, such as, for example, TopLoad packaging. Rondo obaly, on the other hand, focuses on the production of standard folding boxes in large quantities and in the best Rondo quality.

Tripling production capacity
Rondo obaly (“obaly” is the Czech word for packaging) was founded in 2006, with a view to servicing the cost-conscious markets of Western and Central Europe, as well as exploiting the enormous potential in the East – extending as far as Russia. Success is proving that this business decision was the right one. Since then, the plant has been successfully audited by about twenty internationally operating pharmaceutical manufacturers. After only six years in operation, significant expansion measures have been undertaken in the past year. The production area has been expanded to 8000 m² and the production capacity has been increased threefold.
Top quality – even greater safety

These volumes are achieved using the very latest machines. In addition to the two existing MAN printing presses and stamping and gluing units from Bobst, there is now a Heidelberg printing, stamping and gluing line. The new Speedmaster XL 106 can print up to 18,000 sheets per hour and among other things can also provide high-gloss finishes. On the gluing line, inline checking of every box by cameras was a convincing argument for the management of Rondo obaly. Every folding box is compared with the original PDF. Consequently, faulty folding boxes can easily be detected and automatically removed. In addition, an additional code reader identifies an individual data matrix code which is also linked to the original PDF. “In terms of packaging printing we have taken a pioneering route to significantly increase security for our customers”, says Jörg Oswald, Managing Director of Rondo obaly.

Sustainability is key

In the implementation of the structural and technical measures, Rondo obaly paid particular attention to the themes of energy efficiency and environmental compatibility. For example, the waste heat from the printing presses is used to maintain the temperature in the warehouses at a constant level. Energy savings are also achieved by means of a modern lighting system. The required intensity of light can be programmed for each indoor area and controlled depending on the daylight. In addition, Rondo obaly obtains a constant amount of power from renewable sources. The company is FSC and PEFC certified and can therefore offer its customers material from sustainably managed forests.

A good mix

Much is new at Rondo obaly. But the company is proud of one thing in particular: its more than 100 employees, many of whom have been with the company from the very beginning. The vast majority come from the region, but there are of course a number of Swiss and Germans on the team. They are all highly motivated and well trained. Rondo also provides additional facilities for training and re-training which are very popular.

Jörg Oswald outlines the corporate philosophy: “Our Swiss company in the Czech Republic functions so well because all of us, Swiss, Germans and Czechs, constantly have a common goal in mind: to make the best product for our customers!”
SUCCESSFUL PHARMA TECHNOLOGY FORUM 2013 & OPEN HOUSE at Körber Medipak North America

On 12 and 13 March, Körber Medipak welcomed numerous customers, guests and partners from the pharmaceutical industry to sunny Florida for the fourth event of its type.

Photos by: Thomas Große, MediSeal GmbH
Elaiapharm: Late Stage Customisation Centre

Based in South France close to Nice, Elaiapharm is a Contract Manufacturing Organisation founded in 1986, member of Lundbeck group since 2009. The company specializes in oral solids, sterile and freeze-dried products development, manufacturing and packaging. Elaiapharm produces for Lundbeck but also has a strong background working for external customer, which is an important part of the site activity. Strong investments have been done in equipment and utilities over the last years allowing high quality and performance.

Two years ago, Elaiapharm undertook the packaging of an important new solid dose product (Cipralex, an antidepressant) to be launched across a large number of international markets. The product itself is an ODT – orally dispersible tablet – formulation packed in child resistant cold form blisters. The blisters, unprinted at this stage, are manufactured by an external supplier and shipped to Elaiapharm stacked in magazines of 100 blisters each. The focused indication of the product requires packaging in relatively small lots with packaging components specific to each of the markets served. Furthermore, two product strengths and three different counts of blisters per carton must be considered. Elaiapharm sought a solution that would enable the timely and efficient blister printing and packaging of this complex portfolio.

Two years ago, Elaiapharm undertook the packaging of an important new solid dose product (Cipralex, an antidepressant) to be launched across a large number of international markets. The product itself is an ODT – orally dispersible tablet – formulation packed in child resistant cold form blisters. The blisters, unprinted at this stage, are manufactured by an external supplier and shipped to Elaiapharm stacked in magazines of 100 blisters each. The focused indication of the product requires packaging in relatively small lots with packaging components specific to each of the markets served. Furthermore, two product strengths and three different counts of blisters per carton must be considered. Elaiapharm sought a solution that would enable the timely and efficient blister printing and packaging of this complex portfolio.

MediSeal Late Stage Customisation for Packaging Small Lots of Blisters

The Elaiapharm project illustrates the trend towards smaller packaging lot sizes that is certain to accelerate in the coming years. Packaging lots of 5,000 blisters or less become the norm and tiny lots of under 100 blisters increasingly common. The logical end point of lots of single blisters is now conceivable. In the European Union, legislation requires a pharmaceutical product to be labelled and packaged specifically for each of the 27 member states in which it is marketed.

For the conventional packaging process however, small lot sizes mean a serious decline in productivity as measured by OEE (Overall Equipment Effectiveness). The rapidly increasing length of downtime for format changes reduces the utilisation of a packaging line, the running efficiencies are impacted and so the cost per unit of production rises disproportionately. New processes must be considered in order to provide solutions for the efficient packaging of the smallest lots whilst enabling an improvement of the performance of existing assets. The recent rapid advances in digital printing technologies and their application to packaging processes bring new opportunities that make these new processes feasible.
MediSeal call these processes for the packaging of small lots Late Stage Customisation – LSC®.

At the heart of LSC® is the well established MediSeal BIB-BOB system – a means of temporary storage of bulk blisters as work in progress prior to packaging on a mid-speed line dedicated to small lots. The blisters are loaded into the BIB-BOB magazines on a conventional blister line. As is the case here, the magazines may be used to transport the bulk blisters between sites. The blisters may have a standard artwork printed onto their lidding foils during the blistering process or they may be unprinted except for an identifying code. The blisters are then held until required at the small lot packaging line. In the case of Elapharm, the blisters are produced unprinted, except for an alpha-numeric code.

The experience from this line to date indicates typical benefits that a user may realise:

- Several small lots per shift resulting from rapid market changes. Output is measured may be “lots per shift” and not “packs per minute”.
- A revised foil artwork can be implemented immediately after approval.
- The quantity to be produced for each market can be set at the start of the lot: inventories of finished product can be kept to a minimum.
- The LSC cartoning line is operated by a single, qualified operator.

We’d like you to meet…

Victor L. Dixon
COO of Rondo-Pak

Since 1 October 2012, Victor L. Dixon has been President and COO of Rondo-Pak. Victor Dixon brings extensive management experience and numerous successes in the packaging and print business. He was co-founder and CEO of Brandenst, LLC, an innovative startup company for mobile marketing and brand management. Before that, he worked at Catalent Pharma Solutions as manager for the Printed Components division. Victor Dixon came to Catalent from the Cortega Group, a manufacturer of pack inserts, labels and folding boxes for the pharmaceutical industry.

Martin Engels
Managing Director at Seidenader Maschinenbau GmbH

On 1 January 2013, Martin Engels (36) joined the management of Seidenader Maschinenbau GmbH as its Marketing and Sales Director. Mr. Engels has extensive experience in the areas of marketing and sales. Most recently, as Managing Director of DMG Mori Soli Scandinavia, Copenhagen, he was responsible for several national companies and its sales and service staff. Before that he held a senior position in the marketing industry. Mr. Engels studied at Westfälische Wilhelms University in Münster and graduated in Economics, specialising in Marketing.

Lucie Purkertová
Area Sales Manager Rondo obaly s.r.o.

On 1 March 2013 Lucie Purkertová joined the sales team at Rondo in the Czech Republic as Area Sales Manager. She acquired her knowledge of packaging technology at Alinvest Břidličná, where she worked for a total of six years. For the last three years she was employed there as Sales Manager for the Czech Republic and Slovakia. Lucie Purkertová studied at business administration college and is currently taking a correspondence course in Marketing and Management.

Oliver Hecht,
Area Sales Manager Dividella AG

Oliver Hecht (46) joined the sales team at Dividella AG in Grab on 1 January 2013. As Area Sales Manager, one key area of his activity will focus on managing and servicing markets in China and India. Oliver Hecht has many years of professional experience in the design and sales of packaging equipment for the pharmaceutical industry. He studied Mechanical Engineering at the Technical University of Munich.

Lucie Purkertová
Area Sales Manager Rondo obaly s.r.o.

On 1 March 2013 Lucie Purkertová joined the sales team at Rondo in the Czech Republic as Area Sales Manager. She acquired her knowledge of packaging technology at Alinvest Břidličná, where she worked for a total of six years. For the last three years she was employed there as Sales Manager for the Czech Republic and Slovakia. Lucie Purkertová studied at business administration college and is currently taking a correspondence course in Marketing and Management.