

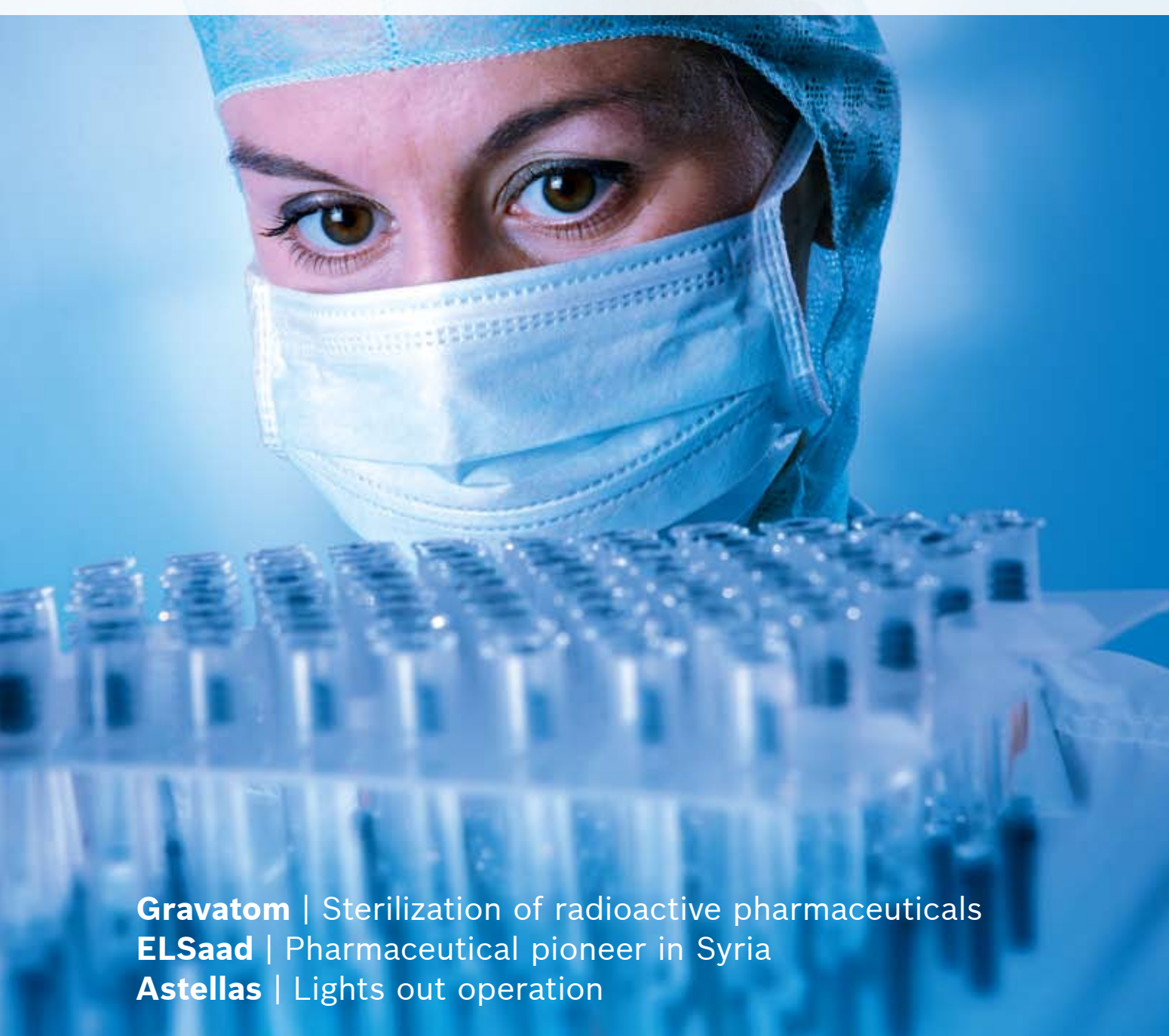
packazine

PHARMA · Issue 02/2008



BOSCH

Invented for life



Gravatom | Sterilization of radioactive pharmaceuticals
ELSaad | Pharmaceutical pioneer in Syria
Astellas | Lights out operation

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Bosch – your competent partner for filling and processing pre-sterilized nested syringes



Dear Readers,

In the world of packaging and processing technology, Bosch Packaging Technology is one of the leading suppliers of single machines, as well as complete solutions. These include services such as audits, or maintenance offers, which improve the efficiency of the equipment throughout its life cycle.

Today, more than ever, customers like to focus on their core competence. They expect from us the competence for processing technology and packaging. Therefore our “one-stop-shopping” concept offers reliable solutions from a single source.

For us, developing solutions means that we recognize market challenges in good time. On the one hand, demand in the pharmaceutical industry is driven by bio-pharmaceutical innovations, demographic changes and the growing markets in the emerging countries.

On the other hand, there are cost pressure increases, which have driven the so-called “total cost of ownership” to become increasingly the foremost criterion in investment decisions. As manufacturers need to lower their costs, while still seeing quality standards rise, safety, high output, flexibility and availability, as well as energy efficiency, are important factors in the pharmaceutical industry.

Customers have trusted Bosch for decades. Our commercial success is evidence of that: compared to the previous year, we have managed to increase our sales volume by 14 percent in 2007, to a total of 650 million Euros. In Asia alone, sales rose to over 100 million Euros. In the future, we expect the willingness to invest to remain consistently high in Asia, Latin America and Eastern Europe, especially with a view to increasing automation.

In this edition we once more present tried and tested developments. You can also experience our system and line competence personally by coming to see us at the most important exhibition in North America: PACK EXPO in Chicago. We'll look forward to meeting you there.

I hope you enjoy the reading.

Friedbert Klefenz

Friedbert Klefenz
President
Bosch Packaging
Technology



Packaging Automation

Creating Better Pharmaceutical and Medical Products with Packaging Partnerships



In the pharmaceutical and medical device industry, more than in any other market, convenience, compliance and safety are critical customer needs driving new innovations. At the same time, brand owners are continuously searching for increased productivity, decreased downtimes, convenience and ease of use, as well as decreased costs through new packaging systems. Like all packaged goods, the new packaging systems must also deliver the best package available to the customer and, furthermore, for non-prescriptive products, must deliver a package that will spark consumer inter-

est as it sits on a shelf. The packaging itself not only impacts the safety and usability of a drug or medical device, it also serves as the primary interface with the patient or medical professional.

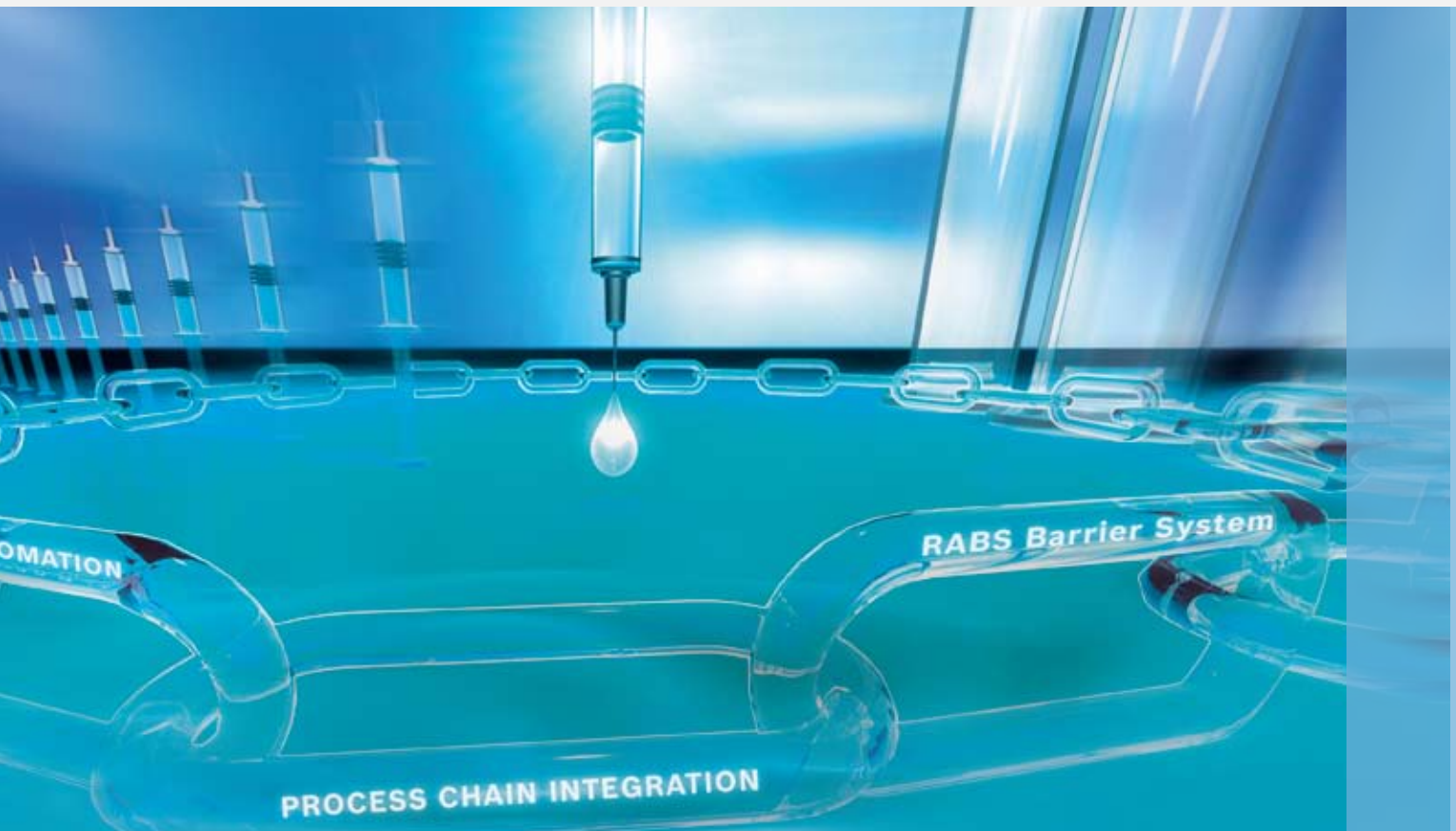
Trends in drug delivery, pharmaceutical, nutraceutical, biopharmaceutical, and vaccine development, as well as cost pressures worldwide have positioned packaging as an integrated process, where automation and engineering partnerships are a necessity to compete effectively. This type of partnership can

elevate overall usability while increasing efficiency and reducing costs.

Redefining compliance and convenience

Convenience in the medical arena is defined by ease-of-use, as well as compliance to correct dosages and dosage combinations. One-time use medical products (for example pre-filled syringes for vaccines, heparin, cardiovascular products and new biotech drugs) illustrate the need for packaging and product to be integrated into one seamless solution.





Bosch began serving the syringe market over 20 years ago, offering high capacity technology that integrates several components into one system. For example, the Bosch **FXS 5100** has increased productivity, as it is capable of filling and sealing up to 36,000 syringes per hour. The pre-filled syringes it produces are conveniently ready-to-use and also meet compliance requirements in terms of dosage levels.

Safety from every angle

Safety is also a key driver, especially in the healthcare industry. Advanced

automation and safety technologies can protect line workers from harmful exposure to volatile substances, while still securing usability of the drug or medical device.

An example of integration of a highly complex pharmaceutical and medical device application comes from Moeller & Devicon. The company developed a single-dose, bowl and nozzle dispenser pack for easy and accurate applications. This type of system requires highly accurate dispensing of an amorphous hydro gel in the filling process and the ultrasonic welding of a dispenser

pack. The entire system needs to be check-weighed and also pressure tested for leaks. In addition, a solution such as this must be protected by means of a restricted access barrier system (**RABS**). This example illustrates how integration and automation of packaging leads to a safer working environment, as well as safer, more accurate products for the medical market.

Working with a single supplier is a good way to seamlessly integrate a line and to streamline automation. Greater automation and integration of packaging lines for medical and health care products is a direct, yet effective way of reducing the total cost of operations, while maintaining a high degree of quality and innovation.

For more information please contact:

Ulrike Probst

Phone +41 52 674 8053

ulrike.probst@bosch.com





Technical Audit

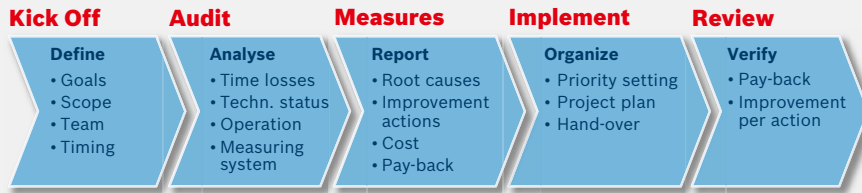
When did your machine last have a health check?

For increasing machine efficiency, Janssen Pharmaceutica relies on the know-how of Bosch Packaging Technology

Janssen Pharmaceutica

Janssen Pharmaceutica is part of Johnson & Johnson, the world's most comprehensive and broadly based healthcare company. Janssen Pharmaceutica, in Belgium, is a worldwide center of excellence of integrated pharmaceutical R&D, production and general services. The company employs over 4,000 specialists at its sites in Beerse, Geel and Olen. Janssen focuses its research activities on medical needs in psychiatry, neurology and cancer, while offering global specialized expertise in pre-clinical and clinical development, chemp-harm development, and chemical and pharmaceutical production.





Nearly all production plants have the same problems: set-up times, waiting for materials, break-downs, downtime, deviations from the planned quantity and idle periods all result in losses which become a considerable cost factor in the long run.

OEE – a revealing figure

The different losses are summed up in the Overall Equipment Efficiency (OEE = availability x level of efficiency x level of quality) rating, a key figure which was created during the development of the Total Productive Maintenance concept. This key figure is getting more and more important, as a high OEE is vital for the productivity and competitiveness of a company.

Optimizing production processes can reduce some of the previously mentioned losses. To be able to do this, the weak points need to be known, as the

causes of the losses are as different as the losses themselves. However, during daily production, it is often not possible to identify and eliminate performance stoppers.

Audit – a recipe for optimization

Our audit is the ideal way to reveal stoppers in your production process and to develop possibilities for optimization. By improving your processes, you can lower costs and save money. For instance, in previous audits, OEE increases of up to 50% have been achieved.

A powerful team

For the successful implementation of an audit, an open dialogue and steady exchange between the team members, consisting of experts from Bosch and the customer, are decisive. At Jansssen Pharmaceutica, the audit team identified considerable potential on an ampoule line consisting of a washing machine, sterilizing tunnel, filling and closing machine. The audit was carried out in accordance with the described process. After the determination of targets, the

line was analyzed during production in order to identify technical and organizational stoppers. Based on the audit report, Bosch created a quotation with coordinated measures for improvement and a comparison of cost and expected use.

Success along the line

The agreed steps were implemented within a short period of time. In the final project review, the success of the audit was confirmed: the introduced measures resulted in an excellent OEE increase on the ampoule line.

As a result of this successful first audit, Janssen had another audit done on a different line.

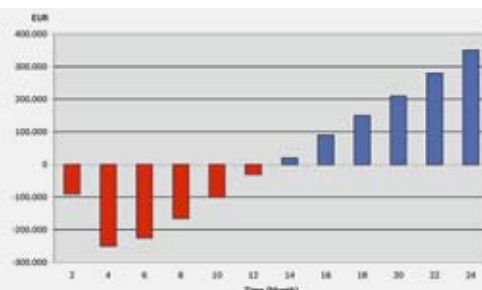
For more information please contact:
Norbert Opaczek
 Phone +49 7951 402 519
norbert.opaczek@bosch.com

Pay-back example

The project cost of e. g. 325,000 € will become due:

- 30 % upon placing the order
- 60 % upon delivery
- 10 % after installation

With an expected ROI of 370,000 €/year i.e. 30,833 €/month, the project will break even after 13 months already.



Know How for the „Hot Cell“

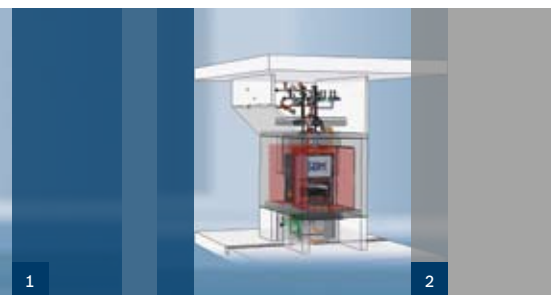
Sterilization of radioactive pharmaceuticals



The French firm CISBIO operates a number of just-in-time production facilities for radiopharmaceuticals all over France. In 2005, it awarded a basic engineering order for the development of a production line to Gravatom, an international engineering company with over 30 years' experience in the development, production, installation and validation of production facilities for the radiopharmaceutical industry. In turn, Gravatom approached SBM, a Bosch Packaging Technology company, with a basic engineering order for a steam sterilizer to be fitted into a radiation-shielded cell.

Radiopharmaceuticals are special tracer substances, which, in conjunction with radionuclides, are used in the diagnostics or therapy of diseases. Given their short half-life these must be produced „on demand“ and used as soon as possible. Due to radiation levels, the manufacturing process has to be conducted in so-called hot cells - areas shielded by lead plates and lead glass. Production, filling and final sterilization are therefore highly automated and outside intervention is only possible by using manipulators.

Following the conclusion of basic engineering, Gravatom was also commissioned to manufacture the fully fitted production unit. At the core of this system is a specially designed sterilizer for final sterilization of the product. For this part of the unit, Gravatom contacted SBM Schoeller-Bleckmann Medizintechnik, a company which had previously delivered sterilizers to CISBIO for a similar project. One of the most important requirements for a sterilizer of this type is that it has to function reliably without requiring servicing. Hot cells, due to radiation levels





inside, cannot be opened until several days after completion of the production process, so any intervention for servicing purposes would delay production for days.

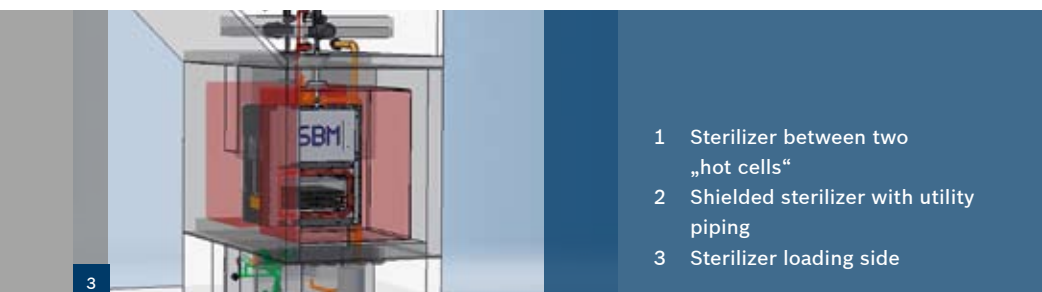
In addition, this project required the sterilizer to be adapted to the particular space conditions inside the shielded unit. Further tasks were the integration of an E-steam generator and the fitting of a sterilizer for loading and unloading using manipulators.

Competent cooperation and optimal customer focus

When starting the project for the engineering order in January 2006, basic specifications as well as close project-related cooperation were agreed. One of the key challenges for this particular project was to design the installation in such a way that changing a door seal, should it become necessary, could be carried out by using a single manipulator. The overall aim was to access the hot cell only once per year for maintenance purposes.

Towards the end of 2006, Gravatom was awarded the production order for the entire hot cell and, in March 2007, SBM received an order for the sterilizer. In October 2007 the FAT for the sterilizer was carried out successfully in the presence of representatives from Gravatom and CISBIO. Some additional modifications were agreed and, finally, in November, the sterilizer was delivered to Gravatom in England where it was integrated into the hot cell in January 2008.

In the course of this sophisticated project, SBM was able to demonstrate its ability as a producer of high-quality sterilizers as well as its successful role as a technology partner, dealing with specific tasks and challenges.



- 1 Sterilizer between two „hot cells“
- 2 Shielded sterilizer with utility piping
- 3 Sterilizer loading side

For more information please contact:

Johann Breyner

Phone +43 2630 312 201

johann.breyner@bosch.com





ELSaad – Pharmaceutical Pioneer in Syria

ELSaad is a Syrian company engaged in the manufacturing and sales of finished pharmaceutical products. Since its establishment in 1995, it has become a leader in producing a broad range of products covering several pharmaceutical areas in the Middle Eastern market.

To continue and improve the production and distribution of its high quality products, ELSaad has expanded its plants in Syria and purchased several fill finish lines from Bosch Packaging Technology. Among them is a high-performance filling line for processing pre-sterilized nested syringes consisting of a **FXS 5100** filling machine and machines for fully

automatic bag and tub opening (**ABO** and **ATO**).

A booming market

When ELSaad was established in 1995, the Syrian pharmaceutical manufacturing market was in its beginnings. At present, the Middle East and North Africa region make up only 2% of global pharmaceuti-

cal sales. However, a growth in population has caused an increasing drug demand, especially for higher-yield pharmaceutical products. That has attracted the attention of multinational Pharma companies. The region now competes with Asian and Latin American countries in terms of the projected growth in its local pharmaceutical industries.

- 1 Fully automatic, loss-free statistical in-process control of the fill weight
- 2 Saad A. Kurdy, CEO ELSaad and Friedbert Klefenz, President of Bosch Packaging Technology



1



2



High performance syringe line with fully automatic bag opening (ABO), fully automatic tub opening (ATO) and filling machine FXS 5100 with integrated In-Process-Checkweigh

Bosch machines strengthen capacity

At the center of the Middle East, Syria serves as a cost efficient location for pharmaceutical production and distribution. With reduced time to market and the determination to serve not only the Syrian market but also the whole Middle East, as well as exporting worldwide, ELSaad started looking for reliable, automatic and high-speed filling machines. These machines will be commissioned in the new plant by the end of 2008.

“Bosch has been offering us reliable machines with high performance and flexibility and because of our existing partnership with them, we bought four filling lines”, says ELSaad CEO, Mr. Saad A. Kurdy.

Among the filling lines, Bosch engineers have specifically developed a high performance filling line for processing pre-sterilized nested syringes, with a high output of up to 500 syringes per minute. The **FXS 5100** series filling machine offers consistent and reliable operation, even at high output levels. Due to servo-controlled motions for the transport system and the Pharma Handling Unit the parameters are stored together as a complete formula that can be reproduced at any time at the push of a button. The line includes an automated bag opener (**ABO**) as well as an automatic tub opening system (**ATO**) for the gentle and low-particle opening of tubs. Satisfied with the high performance and reliability of the Bosch machines, ELSaad projects that the new products to be produced with **FXS 5100** will cover another 5–10% of the Syrian market. He also expects increased exports to other Middle Eastern countries.

Aiming to serve potential markets

According to a survey by the Syrian Ministry of Health, the Syrian pharmaceutical market is worth a potential \$300 million, while the market potential of neighboring countries, Iraq, Jordan and Lebanon, plus North Africa and the Gulf countries reaches \$1 billion.

ELSaad already covers 10% of the Syrian market, and exports to over 25 countries. With its new plant, the company is now ready to export its products worldwide.

For more information please contact:

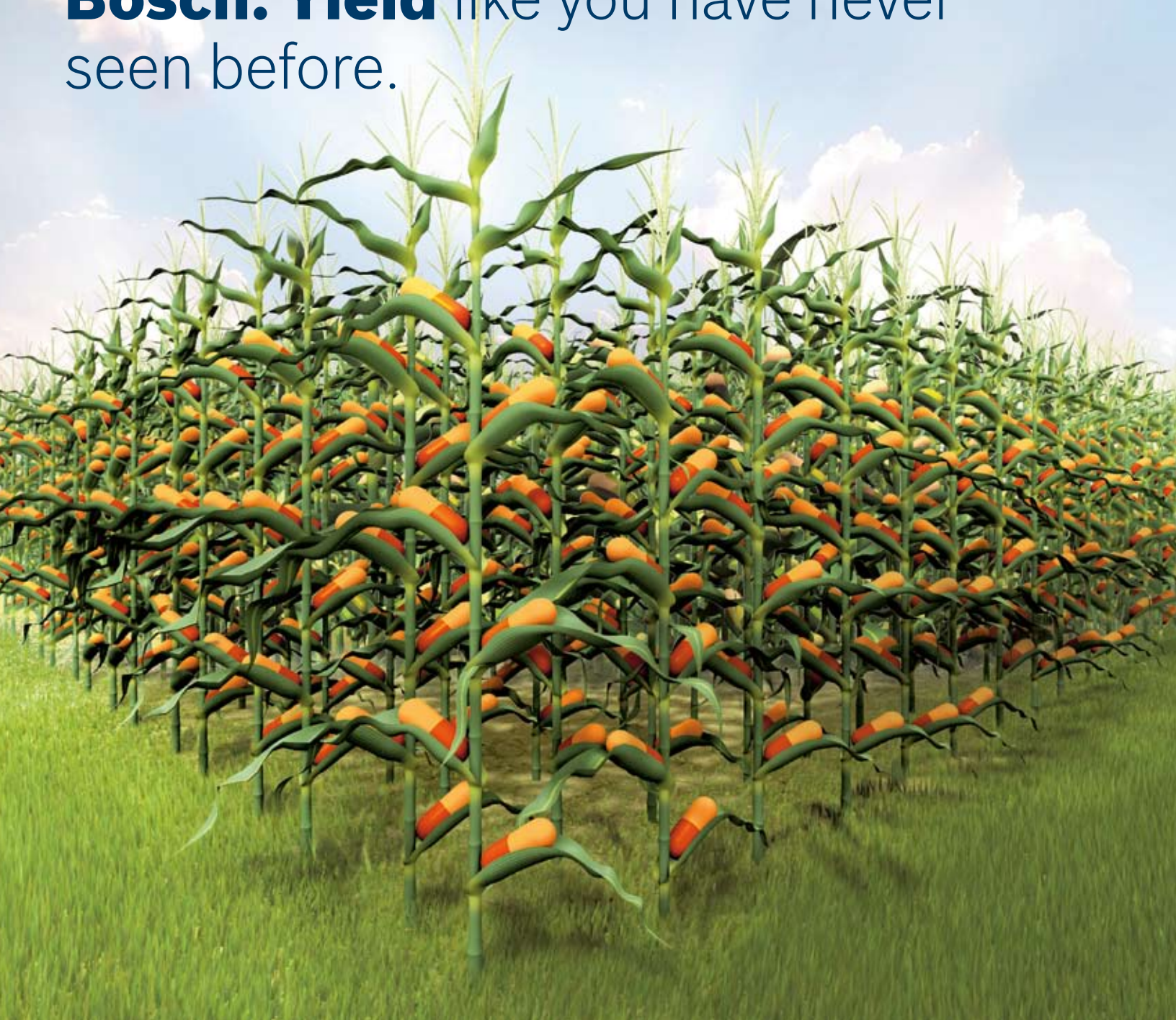
Armin Ziegler

Phone +49 7951 402 646

armin.ziegler@bosch.com



Bosch. Yield like you have never seen before.



Harvest more yield from your capsule filling operations with Bosch GKF capsule filling machines. The quality and reliability of the Bosch GKF with their unique slide gate dosing technology and tamping pin transfer, consistently provide high production yields. Additionally, Bosch service helps to increase your up time and extend the life of your machines. Harvest more yield from your investment with Bosch.



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Robert Bosch Packaging Technology Inc. | USA
Pharma
Phone: +1 763-424-4700
sales@bosch.com | www.boschpharma-us.com

Robert Bosch GmbH | Germany
Pharma Solid
Phone: +49 (0) 711-811-57-147 | Fax: +49 (0) 711-811-57-184
sales.pharmasolids@boschpackaging.com | www.boschpackaging.com

„Lights Out Operation“

Connect and Walk Away

Astellas Ireland Company Ltd has been a Bosch Packaging Technology partner for years, utilizing capsule filling machines and associated peripherals. To meet the requirements of higher productivity, while reducing the total cost of ownership, it has turned to a new “Lights Out Operation” solution from Bosch, which delivers operator free, 24 hour production.

Simply connect and walk away

The lights out operation production at Astellas is achieved through the integrated line components of the Bosch Capsule Filling Line 5 (**CFL5**), with its associated User Management System, an automatic troubleshooting system (**ASB**) and remote control via tablet PC.

The **CFL5** User Management System maps out the critical process parameters, has a line visualization function and lists

potential error sources. The production manager can now sit in the monitoring office and observe the production line, eliminating the need for an operator in an air suit to constantly be near the equipment. As more potent substances are filled and packaged at Astellas, a decrease in the use of air suits and decontamination facilities further minimizes the total cost of ownership.

Additionally, the **CFL5** User Management System controls the line with ease and convenience through a wireless transfer of all component information to the

portable PC. It can be remotely operated and allows the user to see a visualization of the current status of one, or several, modules, as well as allowing remote system adjustments. This allows the user to monitor the system through a simple and easy interface, without being confined to close proximity of the production premises. In addition, the line also has an Overall Equipment Effectiveness function to forecast overall production potential/performance opportunities.

- 1|2 Capsule filling line **CFL3** – little brother of **CFL5**
- 3 Monitoring office for 100% production monitoring
- 4 Capsule flow of full automated capsule filling line **CFL5**





Achieving high performance

The **ASB** function enables the machine to perform several crucial tasks independently, without the need for an operator. It detects blockages caused by deformed empty capsules and automatically removes them. The **ASB** also includes a single capsule discharge that reduces product and capsule loss by not rejecting the entire capsule segment in the event of one failed capsule. This increases automation while lowering the frequency of machine stoppages.

“As soon as the operator starts the machine, we are now able to keep it running unattended, day and night, depending on the capacity of empty capsules,” says Rory McShane, Astellas Project Manager. “The lights out operation has not only enabled us to meet increasing market demand, but it also provides additional production capacity at virtually no extra cost.”

Maximum automation is also achieved through the automatic feeding of capsules and powder, automatic weight checking and regulation, and automatic product sampling.

Partnership boosts leadership

Through lights out operation, Bosch has provided another advanced development for efficient and profitable production. The partnership between Bosch and Astellas has also enabled Astellas to secure long-term, economically efficient production and cements its leadership in capsule filling in the pharmaceutical industry.

For more information please contact:

Felix Nink

Phone +49 711 811 575 26

felix.nink@bosch.com



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