Innovative ideas – innovative solutions

HOF – innovation
HOF R&D Lyo
HOF has established a freeze-dryer for development purposes in its own factory

HOF – products
Success through innovation
Combined HOF unloading system with superimposed sealing machine

HOF – news
HOF’s technical forum 2017: “Always think ahead”
Dear Ladies and Gentlemen

The freeze-drying principle is based on various physical basic principles which, by definition, are not subject to change. However, innovative and continual further developments of technologies around freeze-drying are necessary, in order to guarantee efficiency and safety in the manufacturing process of high-class products. Continual innovations and concepts are arising, particularly in the process area, plant safety and loading and unloading systems. As a machine manufacturer, we want to and have to react to these ever-increasing market requirements.

"HOFInsight" – versatile and informative

With the 1st issue of our new customer magazine HOFInsight, we would like to draw your attention to our innovations, solutions and developments.

With regard to product and plant safety, we are further working on the detection of silicone oil and on the life-cycle optimization of flexible hoses, in order to avoid any case of average. At the same time, we are conducting studies about alternative refrigerants to face the announcement of discontinuation of R404a.

HOF also further optimizes SynchroFreeze, which was developed as a controlled nucleation method.

In our loading and unloading systems segment, a successful concept has been realized in direct collaboration with one of our customers, which consists of a flanging machine working along the unloading area. Thanks to this system, we can save floor space and precious process times.

We are also pleased to announce that this year again, as in 2016, HOF ranks among the Top 100 most innovative companies in Germany.

We hope you are curious now and we look forward to answering your questions about the topics as listed above. We would like to invite you to our technical forum, which will now take place for the second time in November 2017. In this magazine, we will inform you about this event too.

We wish you a lot of success for the future and hope you will enjoy reading the first issue of "HOFInsight".

Sincerely,
the Hof family

TOP 100-Innovator 2017
In 2017 HOF ranks once again among the innovation elite

Following the award in 2016, in 2017 HOF again was awarded with the TOP 100 label and thus ranks among the top 100 most innovative companies in Germany. During a festive support program, all award winners were honored by Mr. Ranga Yogeshwar, the mentor of this competition, with certificate and trophy.

This time again, HOF could particularly score with its innovation management and its accompanying innovation successes. The label itself was awarded for the 24th time in Essen and honores the German innovation elite in different categories.

HOF SynchroFreeze

- Synchronization of the freezing process in the individual vials or product containers
- Conditioning of the product structure
- Improvement of the product homogeneity
- Reduction of required drying times
- Increase of the performance and reduction of the energy consumption

In the pharmaceutical area, the controlled nucleation is a frequently discussed topic. "SynchroFreeze" is a development, well-established by HOF over the last years. Its aim is to provide the user with an additional tool to increase the quality of the pharmaceutical product and simultaneously ensure an efficient operation of the freeze-drying systems. SynchroFreeze is characterized by a conditioning phase, followed by cooling and vacuum-induced nucleation during the freeze-drying process. In the conditioning phase, dissolved gases are withdrawn from the liquid product under partial vacuum, in order to prevent from strong gas bubble formation and swelling of the product in the subsequent freezing steps. The now largely degassed liquid is cooled and the nucleation is triggered by a further pressure drop at the desired freezing point in the lower millibar range (Figure 1).

Product specifications matter

Studies on SynchroFreeze are carried out by different development teams. Application related adjustments of the freezing phase are described within first publications [1]. Conditioning times are different, depending on the product, liquid level and temperature. Moreover, the selection of the freezing point and the subsequent pressure adjustments offer further optimization potential even for difficult products.

In many application cases, a required supercooling can be set by means of the shelf temperature, by reducing the pressure level in the freeze-drying chamber at the same time. After completion of these steps, the product is liquid and put at the required supercooling level.

Optimization of the product structure

A further rapid pressure reduction enables a homogeneous freezing of the vials. The pressure reduction ensures the evaporation of the solvent contents on the liquid surface with local cooling, this triggers the freezing and crystallization process which progresses from the surface downward. Therefore, the adjustment of the chamber pressure enables a rapid and very efficient temperature change at the product surface. In many cases, the targeted application of SynchroFreeze allows the optimization of the product structure (Figure 2 and 3) as well as a significant reduction of the drying times. The larger structure of the lyophilisate simplifies the entry of the solvents and has a favorable effect for the reconstitution process.

The high expectations put to the SynchroFreeze technology are confirmed by the product-specific test results. Furthermore, only limited plant modifications are necessary for the implementation.

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Figure 1: Crystal growth after vacuum-induced nucleation

Figure 2: Lyophilisate structures of a 5% exchange solution, for comparison: left Synchrofreezer – right standard

Figure 3: Scanning electron micrograph; Stylbus product structure after application of SynchroFreeze during freeze-drying


HOF – innovation

HOF SynchroFreeze for optimized freeze drying processes

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Very safe and markedly versatile ...
HOF's loading and unloading systems: successful innovations

Due to the long-term experience, HOF has become the suppliers of future-proof loading and unloading systems. Systems with all degrees of automation can be implemented in many ways, e.g. as an extension of existing freeze-dryers or integrated in newly developed production lines and be upgraded to be state-of-the-art. Through an intensive exchange between customers and HOF's experts, it is possible to achieve a 100% solution meeting each application requirement.

- Combined HOF unloading system with superimposed sealing machine
  A new and innovative system has been developed in collaboration with a renowned pharmaceutical company.

  After the freeze-drying process, the vials are discharged via the HOF unloading system and are subsequently transported into the sealing machine along the unloading system. For this purpose, the system installed in the RABS (Restricted Access Barrier System) individually operates in front of the respective freeze-dryer.

- Your advantages
  - Spatially reduced RABS area
  - Simplified product handling
  - High performance
  - Shorter processing times
  - Reduced running costs

- HOF SMART ACS – new developments currently under scrutiny
  HOF has found innovative solutions to meet the ever-growing requirements in the pharmaceutical area. In the field of loading and unloading systems, new developments have been continually strained in the past: in the sensor technology, hygienic designs, format parts, control system, visualization and system monitoring, in regard to "Industry 4.0". HOF has designed a test plant, especially for this purpose, in order to put in practice all new developments in a target-oriented way.

  This test plant is installed in our facility in Mornshausen and can be used in the future to optimize further processes e.g. in regard of the control system technics.

Optimization of the product safety by means of a relief of the corrugated hoses

Among other components, stainless steel corrugated hoses also belong to the critical parts of a freeze-dryer. These flexible elements transport the silicone oil of the heat transfer system inside the chamber to and from the shelves and are subject to a very high stress level. Due to the fact that these flexible parts are under considerable strain and in combination with the long life time of a freeze-dryer, the corrugated hoses belong to the natural parts subject to wear.

It is very difficult to define change intervals and in case of damage, considerable breakdowns might happen. To counteract this, HOF has developed the so-called "relief shoe". The repeatedly occurring rated break points at the shelf connecting bends are supported by these "relief shoes" and the pressure of the movement is then derived to further hose spirals.

- Your advantages
  - Compared to relief shoe (generation 1)
  - Reduced running costs

- Container Closure Integrity

Because product protection and safety have an ever-growing priority, there are a lot of discussion topics about container closure integrity. It is frequently reported that vial sealing plugs are not correctly or not fully pushed in and therefore the vial sealing is not satisfactory. In many cases, the resulting gap size can be neutralized by the downstream crimping machine, but some uncertainty remains for the time span between opening the freeze-dryer and the actual crimping of the vials with the aluminum cap. These circumstances are usually directly associated with the freeze-drying machine. It must be admitted, that the handmadeshelf area, as a welded construction, is certainly adjusted and ground a number of times, nevertheless a 100% flat surface cannot be reached.

The compliance with the specifications is confirmed by a corresponding certificate. However, major difficulties are met in this context due to variations in the used primary packaging material. Although these differences do range within the specified tolerances, oversize vials impede the sealing of under-sized vials. In order to offer a better understanding of safety in this context, HOF is conducting a study on vacuum tightness with different packaging combinations. An integrity check is carried out at different time intervals on vials which are sealed under vacuum with defined gap sizes. First tests showed that a gap size of up to 1,6 mm, even after a storing time under atmosphere, did not result in loss of vacuum. In order to cover a spectrum as wide as possible, we will go on with our checks, but we are confident that other packaging combinations will deliver similar results.

We will be pleased to keep you in the loop of our results.
With the objective of advancing and testing innovations and technical developments, HOF has established a freeze-dryer for development purposes in its own factory. The so-called R&D Lyo has 5+1 shelves, 1.64 m² shelf area and a 28 kg ice capacity.

A special feature consists in 2 different refrigerating systems: on one side, the heat transfer system of the shelves is operated by conventional refrigeration, on the other side, the condenser is tempered by a technology of natural refrigerants.

Besides many other issues, the further development of both systems is currently a top priority.

More information regarding the R&D Lyo on page 10...
Product safety by means of silicone oil detection

Any leak of silicone oil in the drying chamber means product losses and production losses. In case a leakage is visually assessed, it is in many cases no longer possible to trace back when the silicone oil leak occurred for the first time and we must cast doubt on the quality of many product batches.

Mass spectrometry enables to detect the smallest quantities of silicone oil in the drying chamber, so that any contamination can be immediately identified. Depending on the production concept and on the process requirements, cyclical or continual measurements are made. Currently, we are testing different detection systems at our R&D Lyo, while the limits of the actual method are also checked. At the same time, we are testing the implementation of this technology in existing automation concepts. By means of a defined additional metering of different types of silicone oil, it is possible to clearly identify the corresponding masses. In parallel, optimal test conditions can be observed.

Sustainability by means of natural refrigerants

According to the European F-gas regulation, the use of hydrofluorocarbons (HFCs) must be significantly reduced. Consequently, there are some restrictions in the use of conventional refrigerants. Alternatively, natural refrigerant can be used. Nevertheless, one natural refrigerant alone cannot reach the required temperatures in the condenser. That is the reason why HOF already launched a cascade system in 2007, in which ethane (R-170) and propane (R-1270) are used. This cascade system consisting of 2 separate circuits, forms an individual module, which can be combined with further modules, for redundancy purposes or to improve the performance. Because ethane and propane are combustible hydrocarbons (group A3), the cooling devices are designed according to the ATEX guidelines. Depending on the building concept it is also possible to waive the ATEX requirement if gas detection systems are used.

Retrospective of the 1st HOF’s technical forum of 2014

“Gained in praxis, for the praxis”

On the occasion of the 25th anniversary, HOF Sonderanlagenbau held its 1st technical forum. During the symposium, notable experts from fields of research and industries reported on their recent research results and innovative fields of application in the manufacturing process.

More than 100 attendees came to our site in order to exchange experiences.

Here, you can watch the video about the event:
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