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The efficient planning of temperature-controlled storage for pharmaceutical products

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ABSTRACT

Unlike the planning of conventional warehouses, additional criteria must be considered for storage and material flow planning in pharmaceutical companies. All areas must be qualified from the very start of planning – including the areas of climate control, documentation of storage conditions (e.g. monitoring system), as well as entrance and access control, and particularly for material flow changes in the production area.
The following article examines the success factors for efficient and successful warehouse planning in climate-controlled areas for the pharmaceutical industry.

TEMPERATURE-CONTROLLED STORAGE IN THE PHARMACEUTICAL INDUSTRY

In the pharmaceutical industry, products are associated with very high standards for temperature, storage conditions, clean-room-standards, or compliance with the stipulations of the Narcotics Act and these must be consistently upheld. Legal building codes may be a source of confusion at first glance in this respect, since medications, by definition, cannot be marked as toxic or hazardous in countries like Germany (since this would discourage the patient from taking them). As a result,if toxic or hazardous properties are presentthe requirements imposed must be fully complied with for both storage and transportation. Such requirements are especially relevant when it comes to the separation of inventory due to temperature requirements. It is forbidden to store some materials from various hazard classes, with various toxicity levels, and with other properties together, thus necessitating the establishment of different storage and fire compartments for each temperature range and group of products. The newly created subgroups can cause the minimum number of essential storage areas to multiply – which in turn directly influences the building as well as the logistics and production processes.

The most common temperature classes in the field of pharmaceutical products are ambient/room temperature (15-25°C), cool/cooled products (2-8°C), and frozen/frozen products (not exceeding -18 or -20°C or -25°C). Additional temperature classes become especially interesting, if, for example at temperatures of -40°C or -70°C, limits of feasibility for humans and technology in the daily logistics process are reached. Aside from such special temperature ranges, there is also a trend towards a higher proportion of cooled products whose temperatures are constantly shifting to lower ranges (from ambient to cool for example) and for which compliance must be more carefully monitored (e.g. compliance with temperatures along the entire cold chain, without any disruptions).

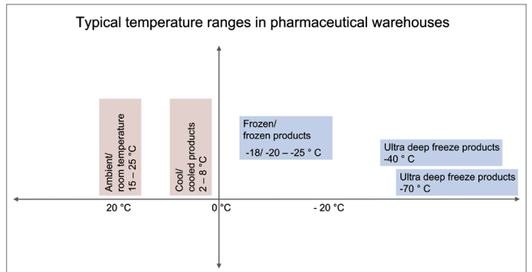

Diagram 1. The proportion of medications that must be kept cool in storage increases.

Starting with the amendment to the GDP Guidelines in the fall of 2013, a difference is no longer recognized between transport and storage when it comes to compliance with temperature criteria. Since the transport area has since become a major focus, the potential of the immobile parts of the supply chain, the processes, and structures in the warehouse, have been given special attention in this article. Efforts are made to clarify this within the initial planning stages, before a warehouse goes into operation. Only those things that are taken into consideration during planning can later be optimally built and operated. It is for this very reason that the requirements for planning a new temperature-controlled warehouse are illustrated. The same requirements apply to existing warehouses and processes, with the only difference being that it is hard to make changes to the status quo once the warehouse has been "set in stone" so to say.

BASIC EVALUATION BEFORE THE PLANNING PROCESS

The database lays the foundation for subsequent operation before planning starts. Only reliable and accurate data can be used to precisely estimate demand in regard to dynamic throughput and static warehouse capacity and then forecast future needs with assumptions about growth and change for each area. In order to ascertain the essential classification properties at all and be able to analyze these in a meaningful way, the requirements for all products within the entire company must be made completely transparent.

Only if the the key data, needs, transport flows, inventory peaks, and throughput peaks are made available in a timely manner (and not, for example, only once the fiscal year is over) the company is able to react proactively – and not reactively. This transparency of the logistics chain is also referred to as "supply chain visibility" (*also see the article by Krebs/Schön about supply chain visibility in the pharmaceuticals industry in TechnoPharm 4 No. 2 102-109 (2014)*). The higher the value of the products, the more important transparency is, especially for (capital-forming) inventory.

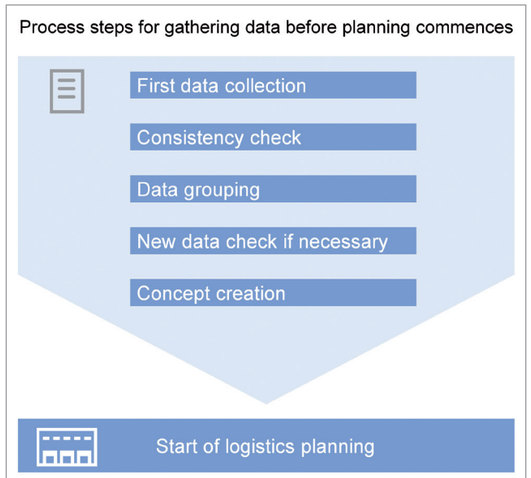

Diagram 2. Process steps for gathering data before planning commences.

The logistics-related question of "make or buy" should also be raised during the initial conceptual planning phases. Especially when a direct connection with the production area is not needed or the product groups to be stored are small and fragmented, outsourcing to a service provider may very well be the most economical solution. The pharmaceuticals sector lags far behind other industries in this respect (*see Miebach Outsourcing Study 2014, "Hype Gives Way to Professionalization"*).

WAREHOUSE PLANNING

The extensive requirements applicable in the area of warehouse-planning make it impossible to address the essential core aspects of pharmaceutical warehouse planning and the associated special concepts and phases in greater detail - but the peculiarities of the various temperature zones and requirements associated with these will be discussed. An explanation of the fundamental concepts of warehouse construction can be found in the article "Warehouse Concepts" (*see Sponheimer article on chaotic warehouse planning in TechnoPharm 2 No. 2 94-99 (2012)*).
The greatest factors influencing temperature-controlled warehouses (aside from the temperature requirements) are typically the hazardous substances, toxic substances, potential risk to waterways, or simply the separation of pharmaceutical products from promotional items or packaging materials. Separation of finished products for distribution from raw and operational materials for production is another important differentiating characteristic for combined warehouses.

Therefore is it crucial, that the data base for temperature-controlled determinations is confirmed prior to the actual planning, considering the logistical requirements.

QUALIFICATION REQUIREMENTS

There is no fundamental difference between the qualification of a temperature-controlled pharmaceutical warehouse and the qualification of other facilities outside of logistics. The combination of buildings, logistical systems, and processes (that may possibly need validation) make it necessary to consider DQ (design qualification). This is because selecting the standards applied as the basis for planning lays the foundation for further planning. During the course of this process validation, all involved planning partners must be aware that the planning parameters used in the pharmaceutical industry may deviate from the "normal" construction standards otherwise applied.
In line with this, conventional construction norms for heating and cooling load calculation (e.g. for Germany: DIN EN 12831 or VDI 2078) are based on statistically backed meteorological experiences that do not constitute hard upper limits. Once these values ("coldest winter" or "hottest summer") are exceeded, however, the planned system will no longer be able to handle the additional temperature difference. Such deviations can easily be accepted in office areas. A qualification of temperature-sensitive areas, however, would fail if insufficient compensation measures are made available. After all, the "standard" parameters to be freely selected in these calculations must also be carefully considered, since workstations (also in the German warehouse) usually require maximum temperatures of 26°C as defined by workplace guidelines, which is a deviation in the ambient range, even when exceeded by only 1K or 1°C.

QUALIFICATION ALSO SUBJECT TO ECONOMIC CONSIDERATIONS

Of course, all GxP-relevant requirements must also be adhered to for qualification. This subheading isn't meant to be a call to "civil pharmaceutical disobedience". When GxP errors occur, however, it can be of economic interest to take a closer look at the type of errors that occur (or that you are looking to avoid) and differentiate between reversible and irreversible errors in the initial risk analysis. Building upon this, the processes can then also be optimized.
If logistical processes are standardized and configured accordingly, however, error minimization and recognition can usually be integrated into normal work procedures. Among other things, this simplifies the tracking and tracing as well as validation processes.
Especially when cold chain must be interrupted, constant process monitoring (that is also integrated into the logistics process) establishes thorough monitoring of compliance with requirements. When it comes to partially finished products in particular, there are many areas where important intermediate steps are required that must be performed (for a short time) outside the cold chain. This could, for example, include the labeling of glass containers, which might involve conditioning the products at higher temperatures to prevent condensation. When product tracking is integrated into logistical processes from the very start, every process can be monitored online. If, in the process, automated warnings are triggered long before critical temperature deviations come into play, this also has the potential to prevent economic losses.

STRUCTURAL AND TECHNICAL PECULIARITIES

A few typical requirements can be identified for this area as well. The most important structural aspects are those that can only be converted with great difficulty later on or not at all. In general, climate control systems should be planned with some redundancy in order to prevent a full system outage in the case that individual components fail. Here the statement "100% redundancy" may sound positive for operational security but can also mean 100% more investments in this area. Gradual redundancy can reduce investments considerably here.
Truck docking stations are another example of this. Loading docks at existing properties can also be equipped with inflatable seals for temperature control later on. The loading ramps at logistics properties are, however, usually designed so that truck drivers must open the doors of the trailer before completing the docking process. This interrupts the cooling chain though, which is why temperature-controlled transports should always be opened only after docking. Corresponding loading bridges must be installed for this, which often requires substantial renovation work on the ramp or the loading yard. Especially highbay warehouses (which can easily reach 40 m) pose additional challenges, since they must be equipped with special climate control and ventilation systems in order to maintain the proper temperature (e.g. to avoid temperature stratification solved by high air exchange rates, jet nozzles, etc.). Since these aspects create considerable problems in the different seasons of the year, a simulation of the temperature distribution in such warehouses also makes sense when determining the configuration of the future monitoring system, especially since adjustments must be made for the differing heating and cooling situations (summer and winter scenarios).
A demanding topic for structural engineering and materials are the "ultra deep freeze" temperatures, e.g. lower than-40°C or even -70°C. Not only do these conditions affect the products being stored, but also the building itself and the equipment installed inside. After a certain settling time, for example, a temperature will establish itself in the walls between two neighboring deep freeze rooms - even when adequate insulation is used - that falls between the two temperature zones of the respective cells. This means that even the structure itself must be capable of withstanding the low temperatures for the duration of its service life.
Especially when it comes to subsequent repurposing of warehouse areas for other temperature zones, these requirements for construction and cooling systems must be taken into account from the very beginning and only very few manufacturers have already obtained the necessary expertise for this.

MODULAR CONSTRUCTION FOR FUTURE FLEXIBILITY

In order to be prepared for any future changes, every plan should be conceived as modularly as possible. This is because creating a "bespoke warehouse" fitting today's needs will be insufficient after just a short period of time once changes arise – and changes occur in every project. This means that, particularly when it comes to material flows, special care must be taken of temperature-controlled areas. Mixed good-in and goods-out areas, meaning places where all temperature classes are processed, are an example of something conducive to process optimization. But this will only work if items are allowed to leave their temperature range for a limited time (e.g. Time out of Refrigeration, TOR).

As soon as (even just single) items need to remain permanently within the cold chain, separate good-in and goods-out must be built for this purpose. If the basic structure of material flows isn't prepared to handle such changes, this results in intersecting material flows with temperature locks along the logistics spine that slows down logistical handling and increases costs.

SUPPORT AND REVIEW OF PLANNING THROUGH STRESS TESTS USING MATERIAL FLOW SIMULATION

To achieve optimal distribution throughout seasonal fluctuations and all known secondary conditions, an extensive material flow and inventory simulation for future warehouse operation should always be used to validate planning. In the best-case scenario, production lines should also be integrated into the simulation. Even if a simulation extends the overall planning time, it minimizes the risk of unexpected situations. In order to achieve this, information such as historical data is combined with expected growth, product changes, and disturbance values (of a technical as well as a developmental nature) to generate a prediction that is as accurate as possible.
The structure of the logistics network, inbound as well as outbound, can also be entered for a simulation and encompasses production locations, suppliers, warehouses, and customers or product recipients.

CHALLENGES ASSOCIATED WITH OPERATIVE USE

A variety of different challenges can arise during operation, depending on the temperature range and process.
Generally speaking, bringing warm products into a cold area (depending on the amount) stresses the cooling systems and neighboring products, which cannot be allowed to warm up through the transfer of heat.
Bringing cold products into a warm area, on the other hand, is more critical for the cold products. Increased humidity in the warmer temperature zones will result in the immediate condensation of moisture on the cold items, which will quickly warm them up while at the same time getting the surrounding cardboard packaging wet. In order to circumvent such impacts, the products can be warmed up in a controlled way in special conditioning chambers (and with dry air) so the packaging will remain in its original condition – and it is best if these chambers have already been taken into account accordingly for the structural planning and logistics processes.

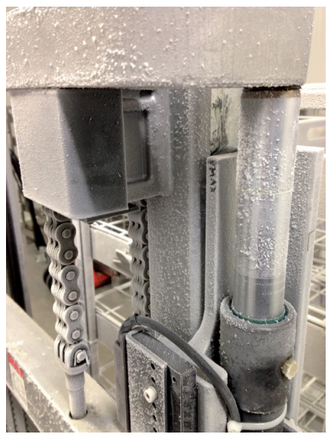

Figure 1. High-lift forklift after three brief stays in the -70°C range.

True difficulties are seen increasingly the lower temperatures are. In addition to the protective equipment required for employees, the material handling equipment used is also put under a lot of stress and in most cases isn't even approved for such ranges by the manufacturer.
The greatest difficulties here arise from physical factors. Furthermore, the most important components (e.g. electrical control components) must be set up in a heatable way to prevent them from freezing. Even when vehicles as forklift trucks are used in "ultra deep freeze range" areas only for a short time, the high temperature difference quickly cools them to the extreme, while reconditioning in a warm area takes considerably longer due to the smaller temperature difference (to the freezing point).
Reconditioning times must always be carefully adhered to, however, since the ice layer created after just a short period of time would otherwise become thicker every time the machine cools down. Any access to the storage area therefore must be very well-planned and prepared, with ad-hoc movements only being allowed in exceptional cases.

SUMMARY

For a temperature-controlled warehousewhich is at the same time efficient and GxP-compliant, a process-oriented overall solution must be the focal point according to the principle "form follows function". Responsibility for logistics and civil construction as well as HVAC should be placed in one hand. Therefore, a general planner must be involved in the project from the very beginning (starting already with the strategic or conceptual phase before detailed design). They will cultivate an awareness of the operative needs as well as the superordinate logistical and production-relevant goals of the company and incorporate these into the current project. Continuity between the completion of planning and start of implementation is the key to successful implementation and efficient future operation without unfavorable surprises. ■

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ABOUT THE AUTHOR

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