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CONTENTS

PLENARY SESSION

I - INDUSTRIAL ENGINEERING

Session 1. Mechanical Engineering

Session 2. Energetics and Process Technique

Session 3. Designing and maintenance

Session 4. Oil and Gas Engineering

II – ENVIRONMENTAL ENGINEERING

Session 5. Health and Environmental protection

Session 6. Environmental Management

Session 7. Occupational Safety

TEMPERATURE MAPPING IN PHARMACEUTICAL WAREHOUSE – FRAMEWORK FOR PHARMACY 4.0

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Abstract: International Society for Pharmacoepidemiology has recently established a specific interest group Pharma 4.0, with the aim of adjusting the pharmaceutical industry to the Industry 4.0 concept. The aim of this study was to select the best strategy for bringing the temperature mapping in the pharmaceutical warehouses closer to Industry 4.0. For this reason, a temperature mapping was performed. Based on the analysis of the obtained results, a choice of optimal locations for continual monitoring was enabled. The human role herein was overseeing the process and reacting should the process could be disrupted. Progressing towards the Pharma 4.0 concept enabled the control of processes guided by the data from the internal sensors, which will in the future guide HVAC system. Relatedly, the way in which the process of controlling environmental conditions in the pharmaceutical warehouses can be automatized as it is outlined in the paper.
Key words: Pharma 4.0; temperature mapping; pharmaceutical industry.

INTRODUCTION

Industry 4.0 is an original project of the German government, which promotes a strategic approach of production digitalization [1]. Herman et al. [2] define Industry 4.0 through four basic principles: IoT (Internet of Things), IoS (Internet of Service), CPS (Cyber-Physical Systems), and Smart Factory.As one of the most profitable industries, pharmacy had to respond and adapt to the emerging challenges. Therefore, ISPE (International Society for Pharmacoepidemiology) creates a special interest group "Pharma 4.0", in order to bring the pharmaceutical industry closer to the concept of Industry 4.0. Pharma 4.0 represents a transformation of the pharmaceutical industry, which includes the collection and analysis of data through "machines", enabling more flexible and efficient processes [3-5]. As the quality of pharmaceutical products largely depends on storage conditions, the qualification of pharmaceutical warehouses certainly represents a process that needs to be improved and brought closer to the Industry 4.0 concept [4]. As part of the Pharma 4.0 recommendations, ISPE has defined 6 phases of digital maturity (Figure 1), from the phase with the least mature elementary informatization, to the phase with the most mature self-managing, intelligent equipment [4-7]. These phases describe the path taken in this research.

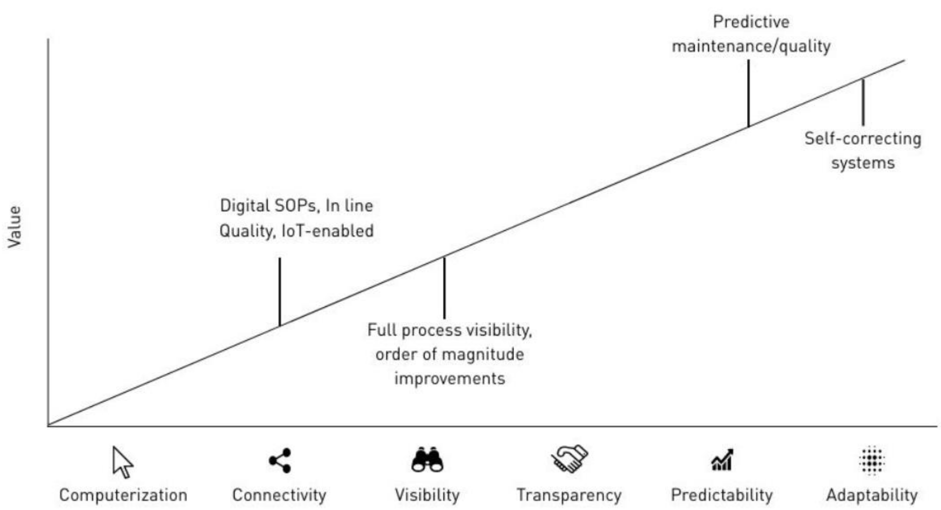

Fig. 1. Stages of digital maturity [7]

Non-compliance with storage conditions is one of the most frequently detected violations detected by regulatory authorities in the pharmaceutical industry during inspections of storage facilities. The most common irregularities concern deviations from the acceptance criteria for ambient conditions, ie. temperature.

Failure to comply with storage conditions can lead to changes in the therapeutic effect of the product, and to harmful effects on the patient's health [8,9]. As temperature deviations are observed during the preparation of raw materials, the production and distribution of pharmaceutical products, a holistic approach to the quality system in pharmaceutical warehouses is needed, which will be based on GMP (Good Manufacturing Practice) and GDP (Good Distributive Practice) [8,9].

The general requirements for the storage of medicines in the pharmaceutical industry, defined by the synonyms "quality system" (GDP and GMP) do not define concise steps for the qualification of the warehouse. Initial temperature mapping, on which we define monitoring positions, cannot prove with certainty the real temperature distribution in the warehouse. The temperature distribution is conditioned by dynamic changes at each point of volume, and represents a very complex thermodynamic task. Li et al. [3] have defined a general methodology for designing wireless sensor networks in order to monitor the production environment in the pharmaceutical plant. Some of their recommendations have been adopted in the research that will be presented in this paper.

RESULTS AND DISCUSSION

Respecting the recommendations, requirements and guidelines established by the relevant regulatory acts [8-13], an experiment of temperature mapping in a pharmaceutical warehouse was performed. Figure 2 shows a diagram of the storage space with the positions where the data loggers are placed. The storage area is P = 2544 m^2, while the volume is V = 35616m^3. The maximum capacity of the storage space is 6782 pallet places. A detailed geometric representation of the mentioned warehouse, as well as the temperature mapping procedure is presented in paper [8]. By collecting and analyzing data, measures for continuous control and monitoring of environmental conditions in real time have been proposed, by which has proven how the qualification process of pharmaceutical warehouses can be further digitized.

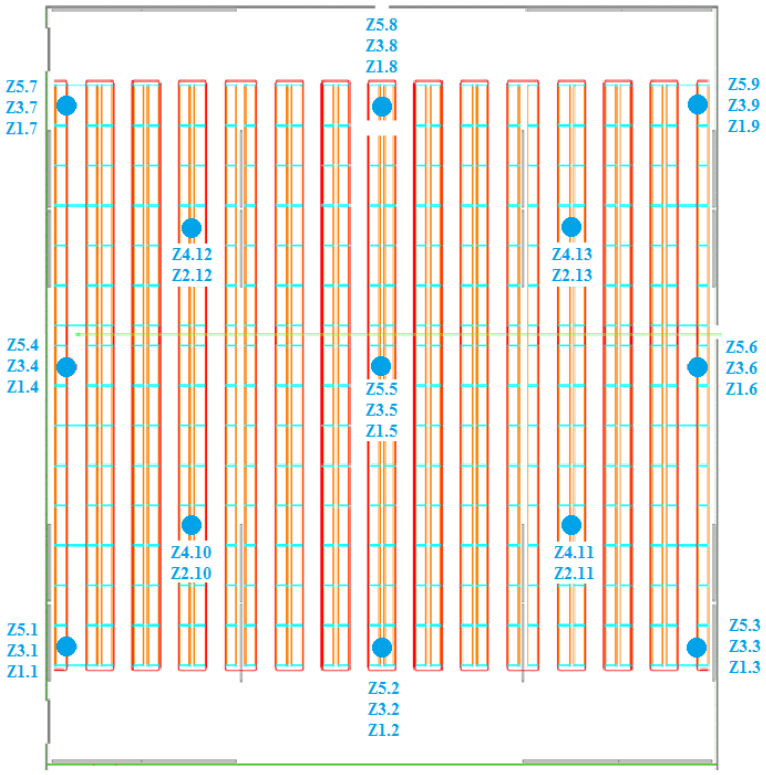

Fig. 2. Data loggers positions

On Figure 2, data loggers are marked in the ZX.Y format where X is the height, and that 1 for data loggers which are set at a height of 1.2 meters from the floor, 2 for data loggers which are set at a height of 3 meters from the floor, 3 for data loggers placed in the central part of the warehouses at a height of 5.5 meters from the floor, 4 for data loggers which are set at an altitude of 8 meters from the floor, and 5 for data loggers placed near the highest storage point, at an altitude of 11.5 meters from the floor. While Y represents the position of the data logger.

Figure 3 shows a graphical representation of the temperature mapping results in the specified pharmaceutical warehouse. In the study conducted in the summer period, 35 data loggers were used, set up according to the scheme shown in Figure 1. Occupancy of the warehouse during the study was ~ 65% (4409 pallets). The temperature mapping test started on July 21, 2017. at 8 p.m, and ended on July 24, 2017. at 8 p.m. The interval between two consecutive measurements was 5 minutes. The outdoor temperature ranged from 20.8 ° C to 40.8 ° C, while the mean outdoor temperature during the summer mapping period was 30.07 ° C.

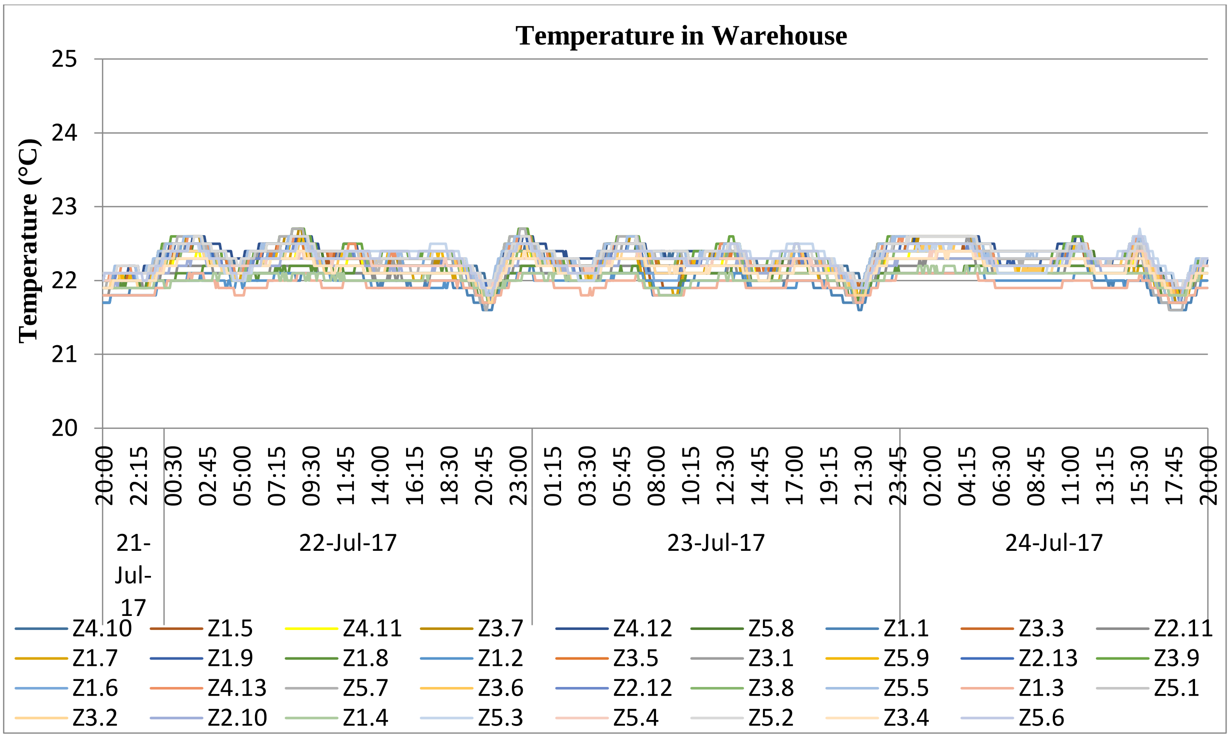

Fig 3. Chart of the data from temperature data loggers

During the execution of the initial study (empty storage), which was shown in paper [8], the temperature ranged from 18.3 ° C to 21.3 ° C, while in this study (~ 65% filled storage) the temperature ranged from 21.6 ° C. ° C to 22.7 ° C, which shows the dependence of the inertia of the system and the occupancy of the warehouse.

After a detailed analysis of the data, the guidelines and regulations require the defining of critical, "warm" and "cold" points. Defining critical points represents the selection of the best positions for internal sensors for continuous monitoring. After the conducted study in the summer, the recommended positions for continuous monitoring are: Z1.1; Z1.3; Z1.9; Z2.11; Z2.13; Z4.11; Z4.13; Z5.2; Z5.3; Z5.4; Z5.5; Z5.6; Z5.7 and Z5.9. This completes the process of mapping the temperature in the warehouse, and as a result, we get positions for continuous monitoring. For the pharmaceutical industry, meeting the requirements of GMP and GDP is inevitable, and the previously performed process of temperature mapping is more than a sufficient approach to meeting the requirements.

By defining critical points, all requirements of standards and regulations are met. Industry 4.0 strives for complete process automation, so an information system that will independently manage the environmental conditions in the warehouse will be proposed below.

Part of the automatic control system is the BMS (Building Management System) as a homogeneous system that collects monitors and stores both critical and non-critical data from the field. Values of all sizes from the project are available on the BMS computer. The concept of this system is to connect physical quantities from the process in three levels: **The peripheral level** consists of all sensors connected to the system on the object, all measurements of temperature, humidity, pressure, operating status, failure, etc.

The controller level consists of all controllers with their distributed modules. In the field of each cabinet there are I / O - modules for accepting the sizes collected in the field. Each of the modules placed in the automation cabinets accepts signals of a certain type. Distributed modules communicate via internal serial P-BUS communication with the controller. All controllers on the high-rack warehouse facility are modular free-programming controllers of the PXC100-D type. The controllers are interconnected in the LON network and communicate with the BACnet protocol.

The BMS level makes up the highest connection level at the high-rack warehouse facility. At this level is the Desigo Insight V5.1 central monitoring and control system. It represents the basic graphical interface to the user. The connection between the controller and Desigo Insight V5.1 is made via the PXG80-N router. The complete topology is shown in Figure 4.

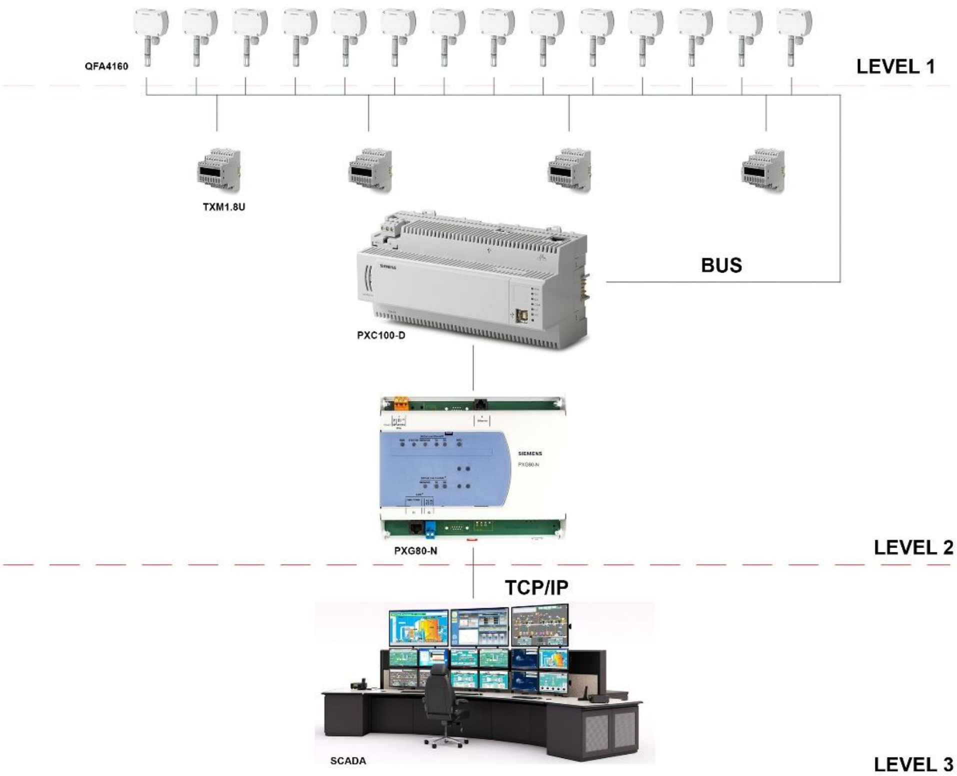

Fig 4. Architecture of distributed control system

With the adoption of the proposed information system, the process of controlling the environmental conditions in the warehouse will be fully automated. BMS collects data from all 14 internal sensors (whose locations are determined by temperature mapping), calculates their mean value and forwards such defined information to the air conditioning system. This enables process control guided by data from internal sensors, which will in the future "guide" the air conditioning system, and shows how the process of controlling environmental conditions in pharmaceutical warehouses can be automated.

CONCLUSION

Although Industry 4.0 represents a progressive leap from traditional automation to a fully integrated and flexible system, the application of these systems in the pharmaceutical industry has not been examined in detail. To reap the benefits, Pharma 4.0 requires further process research, from raw material procurement to distribution to end users. The paper shows how the qualification process of pharmaceutical warehouses could be brought closer to Industry and Pharma 4.0 concepts. Described experiment shows the possibility of defining the optimal number of locations for continuous monitoring, without affecting the quality of drugs which are stored. With the introduction of internal sensors, control of the air conditioning process guided by real-time data is enabled. In addition to continuously providing process control, the ability of analytical data to detect deviations from the required eligibility criteria in a timely manner is very important. Pharmacy is one of the most regulated branches of industry, so this "evolution" should be a great opportunity to demonstrate access and adaptation to digitalization, with the necessary condition that regulatory frameworks become more accessible and open.

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