energy supply. Means and procedures should be in place (in case of possible supply problems) to ensure that the laboratory can continue its activities.

The GPCL Guide contains requirements for all critical aspects of laboratory activities, for example:

- qualification of equipment and validation of analytical procedures,
- risk analysis for measurement quality,
- quality management system (QMS),
- staff competency etc.

The main risk factors for the quality of laboratory measurement results are: personnel, premises, equipment, instruments and other devices, materials, reagents, reference substances and reference materials, calibration, verification of performance and qualification of equipment, instruments and other devices, working procedures, incoming samples, analytical worksheet, validation of analytical procedures, testing, evaluation of test results, certificate of analysis, retained samples and some other.

All these risks need to be systematically identified, assessed and eliminated or minimized with the help of an effective quality system.

The quality management system is aimed not only at ensuring the stable functioning of all processes, but also at continuous improvement due to the systematic analysis and improvement of processes affecting the quality of testing. The QMS should cover planning, risk assessment, auditing, corrective and preventive actions, etc. The QMS is aimed not only at ensuring the stable functioning of all processes, but also at continuous improvement by systematic analysis and improvement of processes that affect on tests. The QMS should cover planning, risk assessment, auditing, corrective and preventive actions (CAPA), etc.

Aim: Development of a set of proposals for the formation of QMS at the domestic laboratories for medicines quality control.

Materials and methods. To carry out our research, we carried out studies on the provisions of GPCL, ISO 9001 and ISO 17025 as part of an overall management system based on the quality risk analysis approach needed to create, implement, operate, monitor, review, maintain and improve of QMS.

Results and discussion. In our work the general algorithm implementation of the system was proposed and developed some sample documents: Quality manual; some standard operating procedures; forms of required entries. We also formulated proposals for the compilation of the basic documentation of the laboratory QMS, proposed are standard job descriptions of personnel involved in the functioning of the laboratory's quality system, and corresponding documented procedures.

Conclusions. Expected changes in the implementation of QMS: operational regulation of activity (system flexibility); minimizing losses of time and resources; improving team discipline; reducing the number of errors and inconsistencies at all levels of the laboratory; improvement of the workflow system; clearer distribution of responsibility; increase employee motivation etc.

DETERMINATION OF RISKS OF PROCESSES OF THE QUALITY SYSTEM OF DISTRIBUTOR OF MEDICINAL PRODUCTS

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Introduction. A pharmaceutical distributor must have a fully developed and properly functioning pharmaceutical quality system, including good manufacturing practices and risk management for quality. This system must be fully documented, and its effectiveness is controlled.

Risk management for the quality of medicinal products is an activity that can not be just a formal fulfillment of the Licensing Terms. It is an integral and very important component of the pharmaceutical quality system. Quality risk management is a systematic process for the overall assessment, control, reporting and review of risks to the quality of the medicinal product during its life cycle.

The ICH Q9 provides guidance on a systematic approach to risk management for quality that facilitates the implementation of the principles and rules of GDP.

In this part of the article, we have focused on the practical implementation of risk management at the distributors of pharmaceutical products.

Aim. To demonstrate, by example, a disturbance of the temperature regime in the premises of the distributor of medicines, the risk analysis by bow tie methods.

Materials and methods. Was used regulatory documents, ISO specialized standards, ICH regulations and other sources of information. The comparative method of analysis the method of structural-logical modeling, the expert method was applied in the study.

Results and discussions. The method of risk assessment – "bow tie" (Bow tie) is a schematic way of describing and analyzing the development path of a dangerous event (temperature disturbance) from causes to consequences. This method combines the investigation of the causes of an event using the fault tree (before the accident) and the analysis of the consequences using the event tree (after the accident). However, the focus of the bow tie method is on the barriers between causes (control measures) and dangerous events and dangerous events and consequences (liquidation measures).

Bowtie diagrams can be constructed on the basis of identified faults and event trees, but more often they are built directly during the brainstorming process.

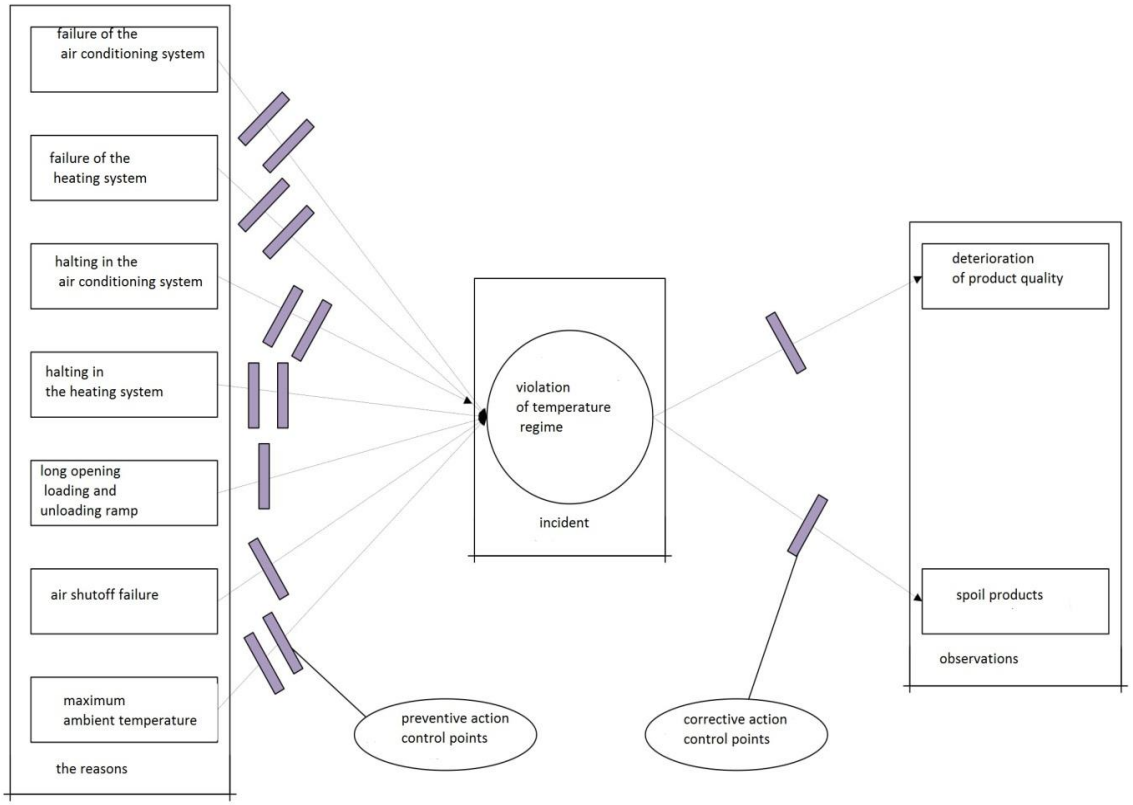

Figure 1 shows the result of the risk analysis of the Bowtie method.

The method of risk assessment based on a bowtie analysis was used to study risk based on the demonstration of a range of possible causes (system failure) and the consequences (damage, reduced product quality). The method was applied in a situation where it is difficult to conduct a complete analysis of the fault tree or when research is more focused on creating barriers or controls for each path of failure.

The focus of the bowtie method is on the barriers between causes (control measures) and dangerous events and dangerous events and consequences (liquidation measures).

Conclusions. We applied the analysis of the "bowtie" diagram to display the risk, indicating a number of possible causes and consequences. Applying this analysis is advisable in the case when there are clear independent ways of development of events leading to failure.

An analysis of the "bow tie" diagram is simpler to understand than the "fault tree" and the "tree" of events, and therefore its use may be appropriate as a means of information interaction in cases where the analysis is carried out using more complex techniques.

PROBLEMS RELATED TO QUALITY ANALYSIS OF HONEY

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Introduction. At present, EU Directive 74/409 of 20 December 2001 has given definition of honey as a 100% bee product, from which nothing needs to be deleted and nothing has to be added. The EU legislation, like the domestic honey standard, is based on the following:

- Pollen study;
- Physical-chemical studies (moisture measurement, Hydroxymethylfurfural, diastases etc.);
- Chromatographical analysis of sugars.

Of these, the first two paragraphs are considered obsolete because of the emergence of new ways of honey falsification, which are difficult to prove. For example, pollen analysis makes it possible to determine not only the naturality of honey, but also its geographical and botanical origin.

However, large processing companies often filter honey using ultrafiltration technology to keep the product in a non-crystalline state for long periods of time. Thus, along with honey, devoid of pollen, and therefore unsuitable for pollen analysis, the market also gets cheap fake honey under the guise of natural.

Aim. Identification of problems related to the analysis of honey quality.

Materials and methods. Often falsifiers add to honey high-fructose corn syrup, close in the sugar content to natural honey. Detection of this type of falsification is based on the complex method of mass spectrometry measurement of the ratio of Carbon $^{13}C/^{12}C$ isotopes. Natural honey has a certain ratio of $^{13}C/^{12}C$, because bees chose as a source of nectar plants with C-3 type of photosynthetic fixation.

Corn, sorghum and sugar cane belong to plants with C-4 type of photosynthetic fixation and therefore have an increased content of the 13C isotope, and consequently, the negative value of the $^{13}C/^{12}C$ ratio. For natural honey it is about -25 ‰, for sugar cane about -11 ‰, for corn a little less – 20 ‰. Detecting beet sugar by this method does not seem possible, because beet belongs to plants of type C-3 and has a ratio of $^{13}C/^{12}C$ at the level -25,5 ‰.

Also, this technique is not suitable for detecting the falsification of honey by products of other plants of type C-3, such as: rice, wheat, barley, rye, potatoes, soybeans. In this case, determine the difference between the content of 13C in honey and its protein fraction. If the deviation of the value in honey to the direction of a C-3 plant is obtained, then the forging of honey can be concluded.

Results and discussion. However, the improvement of honey falsification methods inevitably leads to improved methods of counterfeit detection. For example, in 2002, AV Aganin has developed a method of honey biotesting, which allows simultaneously controlling the freshness, the presence of fermentation, heat damage to honey and falsification. The method is based on the fact that yeast, which is always contained in natural honey, is very sensitive to heating. Instantaneous heating of honey to 70° C followed by rapid cooling completely inactivates yeast, without significantly reducing diastase activity.

To study the sample, the solution of the honey is centrifuged, centrifugate is separated, micropreparation, colored with methylene blue is prepared, and examined under a microscope at 600x magnification. Living yeast cells are poorly colored or not colored at all, dead ones – colored blue.

The results are analyzed as follows: if in the preparation dominate small (0.1-0.2 microns) uncoloured or slightly coloured yeast cells with barely noticeable shell – the honey is fresh and it was not heated; a large