

APPLICATION OF THE GOOD MANUFACTURE PRACTICE STANDARDS FOR PRODUCTION OF FOOD PRODUCTS FOR ASSURING MICROBIOLOGICAL CLEANNESS AND CONTROL OF THE RESIDUES OF DISINFECTANTS

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Abstract

The usage of different disinfectants in the food and pharmaceutical industry provides a possibility for application of certain level of assurance related to microbiological cleanliness by using different types of disinfectants which have different spectrum of operation. Used disinfectants residues which stay on the critical points of the equipment after cleaning become potential contaminants of the products and they can be unsafe for the users' health. Because of this reasons, the Good Manufacture Practice standards recommend validation of the production equipment cleaning procedures including the aspects of microbiological cleanliness and determination of residues of disinfectants.

According to the Republic of Macedonia regulation acts, an application of HACCP system is recommended which will provide safe food with good quality. The methods and control points described in the general principles of this standard are internationally recognized and are from essential meaning. We would recommend in the control of the residues of disinfectants the general principles of HACCP to be used together with the principles of Good Manufacture Practice (GMP) which is well known standard recommended for pharmaceutical production.

The validation plan should include determination of the residue quantity of the disinfectant after cleaning with the disinfectant used. The control method for determination of the residue quantity depends on the chemical characteristics of the disinfectant used. In general, specific methods that are sensitive and give possibility for the detection and quantification of selected disinfectant should be used.

Key words: GMP, HACCP, Disinfectants, Residues.

1. Introduction

A major limitation in the use of disinfectants in the food industry is the fact that food is intended for human or animal consumption. Although disinfectants have the same role as in other industries (i.e. reducing of spoilage and pathogenic microorganisms to safe levels) here they are used in an environment that produces food products. Therefore it is necessary disinfectants to be suitable for their use and they must be non-toxic. This restriction reduces the number of selected used disinfectants on just a few products, of which only a few are sufficiently effective in the presence of organic components. Used disinfectants must be part of a structured sanitary program and the use of it must have to be followed by a cleaning procedure.

The great importance in food production is getting the finished product free of bacterial contaminants (spoilage and pathogenic microorganisms) and other bodies. Contamination of final food products can come from four main sources: the initial raw materials, working surfaces, human factors and air [1].

2. Disinfectants in food industry

In the food industry, cleaning and disinfection are designed to remove all impurities and destroy microorganisms present in the production equipment and packages of final products. These activities must be conducted on products that are contaminated with dirt, germs or residues of disinfectant.

The obtained results of the cleaning procedures cannot be separated into individual results due to the fact that if with the cleaning procedure some quantity of impurities is removed, it means that some of microorganisms are eliminated to certain level, too. This elimination is often not sufficient and therefore proper use and implementation of precise and specified procedures for disinfection is necessary.

Frequently, detergents (alkali) are used concomitantly with other disinfectant (i.e. chlorine derivative) in the form of saline, even some formulations which include quaternary ammonium salts or other products are used to increase power of disinfection procedure.

Contamination of the final food products can often arise from degradation products which are obtained as a result of the degradation that occurred in the product under the influence of heat, moisture, light, oxygen and/or microorganisms. These degradation products, more or less can be mixed with various fungi or molds or other various debris of unknown origin.

Disinfection of food production areas covers equipment, packaging, working surfaces, surfaces of pipes connected to the system, transportation and storage. Products intended for washing and cleaning is necessary to have disinfection effect on production areas and areas where final food products are kept, stored or offered directly to consumers.

The main feature that must be taken, when chemical decontaminating agent is chosen, is the relationship between its solubility in water and lipids. Dirt is a complex of organic and mineral substances and microorganisms. Germs are classified in two great categories: beneficial and harmful bacteria. When they are present simultaneously in the production environment and in final product, there is no possibility to make selective treatment for control of products and therefore, all the living layers are destructed [2].

Commonly used disinfectants are chlorine compounds, which are used in a variety of forms. Many commonly used disinfectants are chlorine free and they are used for disinfection of heavy porous surfaces that come in contact with food. Their purpose and target microorganisms are similar to those of chlorine compounds. These disinfectants are usually efficient enough if surfaces which come in contact with food are previously well prepared, cleaned or rinsed before applying the appropriate disinfectant. Proper design and maintenance of equipment for production and processing of food is essential to ensure contact between active surface, chemical agent and target organisms [3].

The implementation and monitoring of the disinfection procedure has an important role within the sanitation program in each institution of this type. For successful implementation of disinfection, it is necessary that the adopted procedure for disinfection meets several criteria, like: suitable for application in the food industry, non-toxic, safe for use and handling, effective [1].

Although, disinfectants used in the food industry are specifically selected and adequately allowed for their purpose, the potential remains of them on working surfaces and final products are harmful for consumers. They mainly have an adverse effect on the skin, eyes

and respiratory system and adverse impact is mainly expressed if it is ingested, inserted into the human body in overload amount. In the food industry where disinfectants are used, it is especially important to keep an eye on the exposure of personnel to these products, which is stipulated in regulation from 2002, "Control of hazardous substances to health" (COSHH), which demands control of exposure of staff to these substances. Where exposure cannot be prevented, it is necessary to assess health risks and to provide appropriate measures to control use of these harmful substances for health.

The assessment should include a list of all used substances, provided measures to control exposure, which will cover safety in terms of storage, chemical compatibility, used working concentrations, procedures for safe dilution, procedures for safe and reliable application on working equipment. The most commonly used disinfectant in the food industry are groups of surface active agents (surfactants), alcohols, aldehydes, hydrochloric acid and substances that contain organically bound chlorine. According to regulations, "Classification, labeling and packaging of substances and stirring" (GLP), when they are used in the food industry, they must be properly classified and labeled by the supplier [4].

Use of appropriate disinfectant, their maximum and minimum levels for use in food contact surface is regulated by FDA (Food and drug administration) in CFR - Code of Federal Regulations Title 21, 21 CFR 178.1010, Sanitizing Solutions. In some countries, it is acceptable a residue of disinfections to remain on contact surfaces not to be completely rinsed before beginning the production of food, but in most countries this is not the case. Anyways, contamination of final food products with residues of disinfectants is inevitable. Disinfectants, even in low concentrations, can pose a health risk to consumers. Legislation on this issue differs for each country in which the products are manufactured or distributed and therefore it must be regulated by the appropriate state regulatory bodies. Reference standard for minimum acute oral toxicity (for rats) is 2000 mg/kg body weight, accepted for testing the toxicity of substances [1].

2.1 Disinfectants in pharmaceutical industry

According to the requirements of GMP and cGMP the pharmaceutical industry is very strict regarding this issue. One of the more difficult issues which pharmaceutical manufacturers are faced with, especially in terms of the chosen disinfectant is if it is appropriate to its purpose and if its effectiveness is evaluated periodically. The use of resources and procedures for implementation of disinfection, used in the pharmaceutical industry, are defined under applicable ISO standard for

sterile operations (ISO 13408-11) where disinfectants are defined as chemical or physical agents that inactivate vegetative forms of microorganisms, but not necessary and highly resistant spores. This standard can in no way replace national regulatory requirements, set of principles and policies for operating set on GMP regulation and needs [5].

There are many different types of disinfectants used in the pharmaceutical industry in accordance with accepted GMP, with a different range of actions and different activity. The mechanism of action is not always well known and has been reviewed continually. Range of different factors that need to be considered as part of the selection process include the disinfectant method of operation, efficiency, compatibility and compliance with current, reference health and safety standards. That health and safety standards that draw attention to this industry when disinfectants are chosen are the remains of disinfectants on working surfaces and final products.

2.2 Regulations

This is respected in terms of continuing antimicrobial activity and may also lead to the emergence of residual adhesive surfaces which will cause deactivation of the other, the following used disinfectant. Different disinfectants are not compatible with all surfaces depending on the material they are made of. Disinfectants acting aggressively and progressively destroy microorganisms and contribute continuously residues of disinfectants used to be accumulated at these sites, which can be an additional problem. It is necessary for disinfectants to meet validation standards for bactericidal, fungicidal and if it is appropriate sporocidal and virocidal activity.

Within the research project of German Federal Environment Agency about possible health effects from exposure to disinfectants, it is found that only a limited number of active substances are used for most products. Adopted Directive of the European Parliament (EC) No 852/2004 regulates the correct hygiene of foodstuffs that accurately defines all requirements of the food industry that need to be implemented and maintained that are constantly based on principles of HACCP system (Hazard Analysis and Critical Control Points). Disinfectants are included as very important tool (but only one) in HACCP concept. There are many guidelines and technical standards that indicate the importance of hygiene of foodstuffs and managing it, explained in the Codex Alimentarius, a set of international standards adapted the WHO/FAO (1999) [6].

The World Health Organization provides guidelines for a process measures that should be taken to minimize the formation of nus-products of used disinfectants. These guidelines relate specifically to water as an

integral part not only of food industry but also of any other industry. The recommendations of the World Health Organization are as follows [6]:

- Change of process conditions (pH value adjustment, removal of residues of substances previously used)
- Using different chemicals with fewer tendencies to cause residues
- Use of non-chemical disinfection
- Removal of residues prior distribution (e.g. activated carbon, UV radiation, etc.)

Yet according to the World Health Organization every attempt to control the residue of used disinfectant should not compromise the effectiveness of disinfectant. Appropriate means of residual disinfectant can be maintained throughout the distribution system (WHO 2011).

There are many different elements of management measures to mitigate the risk of the used disinfectant which are related to the formulation, authorities, areas of their uses, production, and environment and so on. The purpose of standardization of measures to mitigate the risk is to accept the existing principles for evaluation of biocide active substances and products and to facilitate authorization of final product. Measures to mitigate the risk should be aligned as much as possible at European level to facilitate European market for mutual acceptance of finished products. The adjustments can be set by establishing the standard phases of the mitigation measures of risk, with the precise stages set with precise specifications. European Directive (EC) No 1272/2008 on classification, labeling and packaging of substances and mixtures, replaces previously existing Directive 67/548/EEC on hazardous substances and hazardous preparations 1999/45/EC [6].

Adopted Directive of the European Parliament (EC) No 852/2004 provides in certain parts complete guidelines for food hygiene and producing. The application of HACCP system (Hazard Analysis and Critical Control Points) suggests that the principles of primary production are not yet generally feasible. Guidelines for good manufacturing practices should facilitate the use of hygienic practice on an industrial scale. In particular, these rules apply to primary production to distinguish it from other activities in the industry. For food safety there are several important factors: Regulation must have set minimum sanitary requirements, formal verification of food producers, compliance of manufacturers and distributors of food and it is necessary to be guided by the program and procedures based on the HACCP system. HACCP system should not be considered as a method of self-regulation and it cannot replace the official controls [7].

The use of disinfectants requires strict control regarding Maximum Residue Limits. In addition to the European Directive Article 1 of Directive (EC) 2001/82/EC, Article 2 of Directive (EC) No 882/2004 and Articles 2 and 3 of Directive (EC) No 178/2002, the following definitions apply:

- (1) Residues of pharmacologically active substances cover all pharmacologically active substances expressed as mg/kg or µg/kg on weight, regardless if they are active substances, excipients or degradation products and their metabolites remained in foodstuffs obtained from animals
- (2) Animals used in food production include animals which are bred, raised, kept, and slaughtered for the necessities of food production [8].

Maximum Residue Limits is the maximum concentration of residues recognized by the European Union (EU) in food products derived from animals that have been exposed to veterinary products or biocides. The European Union requires each state to regulate with law that the food products such as meat, milk or eggs obtained from animals treated with veterinary drugs or exposed to biocides should not contain any residues that could reach health hazard to consumers [9].

3. Conclusions

- Regulation in the Republic of Macedonia is set by Law on food safety. Setting limits in terms of residues of chemical substances in food, residues of used disinfectant, means achieving a safe and secure food for end users according to European requirements.
- Law on food safety in the country still does not set normative on production in terms of food production, the maximum residue limits for residues in food and the limits for allowable daily intake of them.
- Control of food producers is essential for public health. Production of reliable and safe food is the most important part for producers as well as for final consumers.

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