Abstract:

A low foaming liquid alkaline and acidic cleaning combinations for use in the cleaning operations of pharmaceutical, food, cosmetic industries, being effective in difficult to remove contaminants, being especially developed for CIP operations, comprising acid or alkalinity sources, a plurality of biodegradable surfactants and biodegradable chelating agent with the surfactant ratio being lower than 4%, the water ratio being higher than 80%. Detergents that are stable throughout their shelf life, low foaming, thus, suitable for CIP applications; comprise biodegradable components that are phosphate free and environmentally friendly; and demonstrate antimicrobial activity. They are appropriate for the applications requiring cleaning validation as the analysis methods of detergent residues thereof can be validated with the known methods.
DESCRIPTION

LIQUID CIP (CLEAN-IN-PLACE) DETERGENT COMBINATIONS

Technical Field
The present invention relates to the liquid detergent composition developed for use in equipment cleaning in the pharmaceutical, cosmetics, and food sectors by means of CIP (clean-in-place) system and the production method thereof.

In particular, the present invention relates to a low foaming liquid CIP detergent composition having an advanced alkaline and acid combination for cleaning hydrophobic impurities from the surfaces and equipments, and an antimicrobial effect and the production method thereof.

Prior Art
Currently, in the detergent industry, detergents with high foaming feature for surface and laundry cleaning are manufactured. The detergents used in washing machines and dishwashers also have high foaming feature; however, cleaning procedures for the same brand detergents used for the same operation deviate due to the deviations in the detergent specifications, leading to changes in cleaning times and consumptions. Residue method validations are not available for cleaning and rinsing operations performed with said detergents. In the cleaning processes of the pharmaceutical, food and cosmetics industries, in order to prevent cross contamination, elimination of impurities as well as cleaner residues is of critical importance.

For the drug manufacturers, performing the validation of the cleaning procedures is required as specified in the following: 1963 FDA GMP Regulations, (Part 133.4), Section 211.67; 1978 CGMP Regulations, Section 211.67; 1993 FDA GMP Inspection Guide; and 2000 ICH Q7. Particularly, in the pharmaceutical, food and cosmetics industries, measurement of cleaning
effectiveness of detergent as well as measuring whether or not detergent residues are present after cleaning is mandatory. At the same time, such industrial type detergents are for domestic use and they are not suitable for use in industry for the CIP purposes.

In the CIP systems, special detergents with the foaming rates being specifically set are used. The main reason for this is to prevent leakage of the foam out of the tank in the cleaning of closed systems while the water and detergent mixture sprayed with high pressure penetrates all parts of said closed systems.

Alkaline detergents help the electrolytic process by increasing the conductivity of the solution. In addition, alkaline detergents increase the cleaning efficiency by enabling saponification of fatty acids. Alkaline detergents are used in the following: hard surface cleaning applications; cleaning and sterilization of production equipments; and CIP applications. However, when the alkaline ratio reaches 30%, the risk of corrosion for the equipments as well as environmental pollution risk increases. In the existing alkaline CIP detergents, the alkaline ratio is above 15%.

In the CIP systems, acid detergents are used in pacification after the CIP application of alkaline detergents and removal of the impurities cleaned with acid. In the detergents with high acidity, risk of corrosion for the devices and equipments is high. Thus, corrosive properties of the acid used in the acid detergent combination should be determined well. Generally, phosphoric and nitric acids are used. These acids are highly corrosive as well as polluting for the environment. In the detergents, at most, anionic and nonionic surfactants are used in combination. However, the toxic effects of the combinations made with nonylphenol group nonionics are high for the environment. Wastes thereof, when mixed with sources of water, leads to foaming and results in difficult degradation, thus, the use thereof is limited or prohibited in many countries.
Another problem of the detergents used in the current state of the art is that they comprise substances such as nitrilotriacetate (NTA) having no biodegradability. NTA is also under examination by the Insecticide Restrictions Action Committee (IRAC) for being a substance with carcinogenic risk (Group 2B). In addition, cleaners used in many detergent combinations and comprising surfactants with no biodegradability are also banned in Europe with the regulation EU 648/2004. Therefore, achieving a high cleaning performance with environmentally friendly and safe combinations has become a necessity.

Studies in the literature on the subject matter comprise many detergent combinations and application methods developed for use in CIP systems. One of them is the application JP2007326944 with the title 'Deodorant composition for CIP system and method for the application thereof. Said study with high storage stability and low foaming feature is developed for preventing the damage to the equipments used in the food and beverage production and the odors that may occur in the packagings. Said deodorant composition comprises a water soluble solvent, sugar, alcohols, polymers, water as well as a nonionic detergent and solvent.

Another application filed on the subject matter is the NZ553326 document with the title 'Use of the liquid detergent comprising fatty alkyl-1,3-diaminopropane in CIP systems'. In said study, a detergent combination with a pH value ranging from 0.1 to 5 comprising the following is disclosed: the fatty alkyl-1,3-diaminopropane having the general formula of R-NH-CH2CH2CH2NH2 or salt thereof, wherein the R mentioned in the formula is a C4-C22 alkyl group. Another application encountered in the literature is the JP2005200627 with the title 'Cleaner composition used in CIP systems'. In said application, again, minimizing the detergent residues and reducing the contamination is aimed with the developed cleaner composition and in order to provide solutions to
these problems, a composition having a SP value of 6 to 9 at 25°C and C5-C24 hydrocarbon and nonionic surfactants is developed.

Another application is the JP201 1252160 with the title 'CIP cleaning method'. Said CIP detergent composition is also used for removal of odors, wherein it comprises the following: a nonionic surfactant content ranging from 0.01% to 30% and selected from the group consisting of polyoxyalkylene fatty acid ester, polyoxyalkylene sorbitan fatty acid ester, sorbitan fatty acid ester, polyoxyalkylene sorbitol fatty acid ester, glycerol fatty acid ester, polyglycerol fatty acid ester, polyoxyalkylene glycerol fatty acid ester, polyoxyethylene-polyoxypropylene block polymer, reversible type polyoxyethylene-polyoxypropylene block polymer, polyethylene glycol fatty acid ester, propylene glycol fatty acid ester, polyoxyalkylene alkyl ether, sucrose fatty acid ester; an defoaming agent ranging from 0.09% to 10%; and water.

Another application is the JP201 021 5780 with the title A detergent composition for CIP systems and a washing method developed with the use thereof. In said application, development of a detergent composition having the following features is aimed: removal of organic residues such as food and beverage residues resulting from heat denaturation; and low foaming. Following is provided in the content thereof: 5-30 wt% alkali metal hydroxide salt, 0.5-5 wt% chlorine oxidant, 1-7 wt% silicate, 0.5-7 wt% phosphonate, 0.1-5 wt% amphoteric surfactant and water for blending the mixture.

Consequently, detergent combinations used in the CIP systems and production methods thereof are improved, thus, new structures, which would eliminate the aforementioned drawbacks and offer solutions to the existing systems are needed.

**Brief Description of the Invention**
The present invention, meeting the aforementioned requirements, eliminating all the drawbacks and bringing additional advantages, relates to the liquid
detergent composition developed for use in equipment cleaning in the pharmaceutical, cosmetics, and food sectors by means of CIP (clean-in-place) system and the production method thereof.

The present invention comprises an advanced alkaline and acid combination for cleaning hydrophobic impurities from the surfaces and equipments. In addition, it comprises a low foaming composition suitable for CIP systems and it shows antimicrobial activity. Liquid cleaner combinations of the present invention are combinations of a source of acidity or alkalinity and other environmentally friendly, i.e. biodegradable components. As a result of the structural modification (transformation) of the biodegradable components by the microorganisms, main structure of the substance is degraded and subsequently, properties thereof are lost.

In the primary degradation of all the detergent active ingredients entering the combination according to the present invention: The surfactants contained in the product are on average at least 90% biodegradable in accordance With the requirements of the European Union Mandatory Standards for Detergents 82/242 (nonionic surfactants).

In the final biodegradation: they degrade fast and easy and in the total organic content reduction tests of the product following values are attained: > 60% BOD/COD or CO₂ release of > 70% COD reduction. For easy degradability, initial values are reached (OECD Method 301).

The specific test methods of the surfactants for determining the property losses of the substances are listed in the Anex 11 of the 'Official Journal of the European Union' August 4, 2004 (Article 2, Definition 6 and 7). In the composition of the developed CIP cleaning detergents, surfactants as well as chelating agents are biodegradable.
Detergents are combinations of ethoxylate based nonionic detergent active ingredients. Detergents comprising compounds containing phosphorus is an advantage. Phosphorus is an essential nutrient for the growth of plants and when present in large amounts in water, it leads to eutrophication or excessive algae growth and significantly decreases the water quality. Detergents do not contain silicate. Because silicates are toxic to aquatic organisms and they do not undergo biodegradation. Moreover, they do not contain the corrosion inhibiting silicate-phosphonate combination either.

The maximum utilization rate of the elements leading to corrosion is limited as 4% and sodium chloride is used as stabilizer and corrosion inhibitor. In the existing high alkaline detergents, pH is over 13 for the dilutions prepared with 1/100 deionized water, while the pH of the alkaline detergent according to the present invention is below 12 for the same dilution. At the same dilution, conductivity is measured over 25.5 mS for the existing CIP alkaline detergents, while the conductivity of the detergent according to the present invention is measured as 1.4 mS.

In the existing acid (phosphoric and/or nitric acid) detergents, pH is below 2 for the dilutions prepared with 1/100 deionized water, while the pH of the alkaline detergent according to the present invention is 3 for the same dilution. At the same dilution, conductivity is measured as 0.6 mS for the detergent according to the present invention. Conductivity is above 6 mS for the existing phosphoric or nitric acid based CIP acid detergents. The present invention shows conductivity values that are 1/10 of the existing acid detergents. This situation prevents the risk of corrosion.

Another advantage of the present invention is that the product shows antimicrobial activity due to the microbicidal activity of the quaternary ammonium compound benzalkonium chloride being used as stabilizer. In particular, this situation provides the user with both time and cost savings as
an additional disinfection operation after the cleaning operation is not required.

The structural and the characteristic features and all advantages of the present invention will be understood more clearly with the following figures and the detailed description written by referring to said figures and therefore, the evaluation needs to be done by taking said figures and detailed description into consideration.

**Detailed Description of the Invention**

In this detailed description, the liquid CIP detergent composition and the production method thereof according to the present invention and the preferred embodiments thereof are described only for a better understanding of the subject without constituting any restrictive effect.

Following is used in the alkaline CIP detergent formulation of the liquid CIP detergent combination according to the present invention: preferably <1% fatty alcohol ethoxylate (C12-C14 + 6 EO), <2% butyl end-capped fatty alcohol, C12/18-10 EO, ethoxylate. Cationic detergent active ingredient, <0.2% alkylbenzyl dimethylammonium chloride, is used in the formulation as stabilizer. <0.5% sodium chloride and <0.02% sodium edetate are used as buffering and chelating agents, respectively and <0.5% citric acid is used as pH buffering agent. 1-5% sodium hydroxide is used as alkaline agent.

In the present invention, sodium hydroxide or potassium hydroxide, or a combination thereof can be used as pH adjuster. Sodium hydroxide is preferred due to being a source of the alkalinity as well as for the antimicrobial effect thereof. Sodium hydroxide, alkalinity source, is an EPA-approved 'active' ingredient, i.e. activity thereof against microorganisms is approved. Sodium hydroxide has been approved by the United States Environmental Protection Agency (EPA) for being used in many cases as herbicide, fungicide, algaecide and disinfectant (EPA R.E.D. Facts for
Sodium Hydroxide, EPA-738-F-92-008, September 1992). In addition, sodium hydroxide is not only an alkalinity agent for the formula but also a cleaning performance enhancer by the effect thereof on the solubility and alkaline hydrolysis (saponification). It is used together with the 0.05-0.5 wt% citric acid in order to provide chemical stabilization of the 1-5 wt% sodium hydroxide. As a result, alkalinity sources demonstrate not only effective cleaning characteristics but also disinfectant properties.

As stated above, in the selection of the one of the most important parts characterizing the present invention, the surface tension reducing agent of the liquid detergent active ingredient, i.e. surfactant, following detergent active ingredients demonstrating high cleaning activity at low detergent doses for cleaning the drug residues are preferred: water containing, no foaming, fatty alcohol ethoxylate based C12/18 - 10 EO n-butyl end-capped chain detergent active ingredient; and low foaming, fatty alcohol ethoxylate based C12-C14+6 EO detergent active ingredient. In the water containing, no foaming fatty alcohol ethoxylate based C12/18 - 10 EO n-butyl end-capped chain detergent active ingredient and low foaming, fatty alcohol ethoxylate based C12-C14+6 EO detergent active ingredient: The surfactants contained are on average at least 90% biodegradable in accordance with the requirements of the European Union Mandatory Standards for Detergents 82/242 (nonionic surfactants) and the 82/243/EEC. They degrade fast and easy. In the total organic content reduction tests of the product following values are attained: > 60% BOD/COD or CO2 release of > 70% COD reduction. For easy degradability, initial values are reached (OECD Method 301).

Biodegradable sodium chloride (NaCl) and sodium edetate are used as chelating agent in the liquid alkaline CIP combination according to the present invention. Chelating agents interact with the metal ions that can be contacted during use of the composition. Thus, chelating agents contribute to
the cleaning performance of the present invention as well as to the hard water tolerance.

In the formulation, quaternary ammonium based cationic detergent active ingredient benzyl-dimethyl-tridecyl-azonium chloride and/or alkyl dimethybenzyl ammonium chloride is used as stabilizer. Ordinary surfactants used in cleaning products tend to degrade over time due to high acidity or alkalinity and therefore they are not capable of serving as stability indicator throughout the product's shelf life. The present invention overcomes the tendency of the disinfectant active ingredients being unstable in the alkaline solution. <0.5% quaternary ammonium based cationic detergent active ingredient is used as stabilizer and <0.5% citric acid is used as stabilizer and antioxidant.

The detergent active ingredient ratio for the alkaline detergent is 2%. Combinations of 1-5% can be formed. Such combinations have a high cleaning activity. Foaming rate is formed as the liquid detergent volume and it is suitable for the CIP detergent.

The detergent active ingredient ratio for the acid detergent is 0.2%. 5% citric acid is used as acid source, 1% sodium chloride is used as stabilizer and buffer, and 0.2% sodium EDTA is used as chelating agent.

The alcohol ethoxylate nonionic detergent active ingredients C12-C14 + 6 EO detergent and C12/18 - 10 EO n-butyl end-capped chain detergent active ingredient are combined together with a ratio of 1 to 3. Optimal foam control and cleaning power is provided with this combination.

The detergent combinations according to the present invention do not comprise coloring agents and viscosity agents. Density of both the alkaline and acid CIP detergents are about 1.0 g/cm³. The detergent does not cause
unnecessary contamination as it does not contain the chemicals other than the main ones affecting the activity thereof.

When the alkaline CIP detergent production is examined on the basis of 1000 ml of product; 5 g nonionic surfactant fatty alcohol ethoxylate C12-C14 + 6 EO is added into 900 ml of soft or demineralized water and mixed at ambient temperature under stirring. After the completion of the dissolution, 15 g of the other nonionic surfactant, water containing, no foaming, fatty alcohol ethoxylate based C12/18 - 10 EO n-butyl end-capped chain detergent active ingredient is added and stirred until dissolved. Then 25 g sodium hydroxide (NaOH) is added, stirred and dissolved.

After these, 2.5 g salt-sodium chloride (NaCl), 8 g citric acid, 11 g of 50% benzalkonium chloride solution are added successively and one at a time, mixed and dissolved. The mixing process is continued until the turbidity of the detergent solution is completely removed. Then, 30 g of sodium edetate is added and stirred until being dissolved. Then, volume of the solution is checked and if necessary the volume is completed to 1000 ml by the addition of soft water or demineralized water. The pH value of said solution is about 13.2.

When the acid CIP detergent production is examined on the basis of 1000 ml of product; 0.5 g nonionic surfactant fatty alcohol ethoxylate C12-C14 + 6 EO is added into 900 ml of soft or demineralized water and mixed at ambient temperature under stirring. After the completion of the dissolution, 1.5 g of the nonionic surfactant, water containing, no foaming, fatty alcohol ethoxylate based C12/18 - 10 EO n-butyl end-capped chain detergent active ingredient is added and stirred until dissolved.

50 g of anhydrous citric acid is added into said mixture and dissolved under stirring. Then, 10 g salt-sodium chloride (NaCl) and 2 g sodium edetate are added and dissolved under stirring. Volume of the solution is checked and if
necessary the volume is completed to 1000 ml by the addition of soft water or demineralized water. pH value of the detergent solution is found to be less than 2.

As stated earlier, the CIP detergents enable establishment of the effective cleaning procedures with minimal corrosive impact as they are specific to the pharmaceutical, food and cosmetic industry equipments. Alkaline or acid detergents can be used with the dilution range of 1/25 to 1/200. In addition, the temperature of the water that can be used therewith can be in the range of 25 to 80°C. Dilution ratio is set according to the pollution degree of the equipment and the hardness of the water to be used for dilution. In the case of hard water, more intense dilutions in the range of 1/25 to 1/100, while in the case of soft water, dilutions in the range of 1/50 to 1/200 depending on the pollution levels are appropriate.

When the CIP detergent combinations according to the present invention are applied to numerous substrates, excellent cleaning quality is obtained. They are used for CIP or cleaning out of place (COP) of the following substrates: For instance, chemical reaction tanks, pharmaceutical containers and equipments, medical equipments, equipments used in milk, canned food, fruit juice and meat industries, food production equipments, equipments used in the manufacturing of cosmetic materials such as hair dye, creams, lotions, sun lotions, aftershaves, etc. The CIP detergent combinations according to the present invention are suitable for tanks and equipments of the pharmaceutical, cosmetics and food industries when used with the dilutions in the range of 1/25 to 1/200. They can be used for the food industry in cleaning of pipelines, closed system circulations.
When the pH values at various utilization dilutions are examined:

For the alkaline detergent following pH values are observed: 12.4 at 1/25 dilution, 12.0 at 1/50 dilution, 11.8 at 1/100 dilution, and 11.5 at 1/200 dilution.

For the acid detergent following pH values are observed: 2.2 at 1/25 dilution, 2.5 at 1/50 dilution, 2.8 at 1/100 dilution, and 3.0 at 1/200 dilution.

When the conductivity values of the alkaline and acid CIP detergents are examined:

For the alkaline CIP detergent following conductivity and pH values are observed: 55.4 pS, pH: 9.58 in a total of 10 ppm alkaline detergent active ingredient/deionized water, 30.2 pS, pH: 9.00 in a total of 5 ppm alkaline detergent active ingredient/deionized water, 15.64 pS, pH: 6.93 in a total of 2.5 ppm alkaline detergent active ingredient/deionized water, 7.70 pS, pH: 6.65 in a total of 1.25 ppm alkaline detergent active ingredient/deionized water, and 60 μS, pH: 6.50 in a total of 1 ppm alkaline detergent active ingredient/deionized water.

For the acid CIP detergent following conductivity and pH values are observed: 374 pS, pH: 3.14 in a total of 10 ppm acid detergent active ingredient/deionized water, 104.4 pS, pH: 3.63 in a total of 2 ppm acid detergent active ingredient/deionized water, 31.8 pS, pH: 4.14 in a total of 0.5 ppm acid detergent active ingredient/deionized water, 7.66 pS, pH: 4.72 in a total of 0.1 ppm acid detergent active ingredient/deionized water, and 3.98 pS, pH: 5.12 in a total of 0.05 ppm acid detergent active ingredient/deionized water.

Residues of the detergent active ingredients can be analyzed by HPLC with UV detector. It is necessary to prove that the detergent residues are
eliminated after the cleaning of the equipments of particularly the pharmaceutical industry, cosmetics and food industries. For this purpose, residue testing is performed by the analysis of rinse water samples with devices such as HPLC and TOC.

In the quantitative determination method by HPLC of the nonionic alcohol ethoxylate detergent active ingredients used in the present invention, following is performed:

In the standard preparation: 150 mg C12/18 - 10 EO, n-butyl end-capped chain alcohol ethoxylate detergent active ingredient standard and 50 mg fatty alcohol, alcohol ethoxylate based detergent active ingredient C12-C14 + 6 EO detergent active ingredient standard are weighed into the 25 ml volumetric flask. It is kept in a water bath at a temperature of 80°C for 20-30 minutes after weighing 500 mg maleic anhydride and 300 mg urea therein and adding 10 ml of distilled water.

Derivatization of the detergent active ingredients is provided during the holding at this temperature. The volumetric flask removed from the water bath is cooled to ambient temperature. When the cooling is finished the volume is completed with the MeOH / 0.1 NH₃·2/1 mixture. 1/2 and 1/4 dilutions of the prepared standard is performed with the mixture MeOH / 0.1 NH₃·2/1 . Standard solutions of approximately 8 mg/ml, 4 mg/ml, 2 mg/ml are filtered through a 0.45 μm filter and reading of the three standards is carried out on the device.

In the sample preparation: 500 mg maleic anhydride and 300 mg urea are weighed into the 25 ml volumetric flask and 10 ml alkaline detergent is added thereon. It is kept in a water bath at a temperature of 80°C for 20-30 minutes. Derivatization of the detergent active ingredients is provided during the holding at this temperature. The sample removed from the water bath is cooled to ambient temperature. When the cooling is finished the volume is
completed with the MeOH / NH3: 2/1 mixture. Approximately 4 mg/ml of the sample solution is filtered through a 0.45 µm filter and introduced into the HPLC (high pressure liquid chromatography).

Mobile Phase:
A: Acetonitrile (ACN) 100%
B: Glacial Acetic Acid 0.1% w/v

Gradient program:
0.00 B Cone. 50%
45.00 B Cone. 5%

Chromatographic Conditions:
Column: C8, 4.6 x 250 mm, 5 µm
Low Pressure Gradient
Solvent B Cone. : 50%
Column temperature: 35°C
Analysis Duration: 50 min
Injection volume: 20 µl Flow Rate: 1.5 ml/min

Method validation parameters
Detergent active ingredients by number of carbons Calibration curve ID1: C12
Detergent active ingredients by number of carbons Calibration curve ID2: C14

Table 1: Method validation
ID1: C12: RF%RSD 5.61 (Relative standard deviation), LOD (Limit of Detection): 0.13, LOQ (Limit of quantitation): 0.39, Accuracy %: 0.83

ID2: C14: RF%RSD 1.94 (Relative standard deviation), LOD (Limit of Detection) 1.94: 0.10, LOQ (Limit of quantitation): 0.31 Accuracy %: 0.72

Table 2: HPLC device analysis page
CLAIMS

1. A disinfectant, low foaming, liquid alkaline cleaning composition, which is suitable for CIP use, can be validated with the known determination methods and comprises the following:
   - 1-5 wt% alkalinity source based on a total weight of the combination, 0.01-1 wt% quaternary ammonium compounds as stabilizer based on the total weight of the combination,
   - 0.1-1 wt% biodegradable C12-C14+6 EO alcohol ethoxylate based detergent active ingredient, based on the total weight of the combination; 0.5-2 wt% biodegradable C 12/18 - 10 EO, n-butyl end-capped chain alcohol ethoxylate detergent active ingredient based on the total weight of the combination,
   - 0.01-1 wt% organic acid as an antioxidant and a stabilizer based on the total weight of the combination, 0.1-1 wt% sodium chloride as buffering agent based on the total weight of the combination, 0.01-0.5 wt% sodium EDTA as chelating agent based on the total weight of the combination; and
   a low foaming acid detergent combination which is suitable for CIP use, can be validated with the known determination methods, used by being diluted with water at ratios of 1/100 - 1/500 and comprises citric acid as acidity agent and sodium chloride as a buffer and/or buffering agent.

2. Liquid alkaline cleaning composition according to claim 1, characterized in that, said alkalinity source is sodium hydroxide and potassium hydroxide (100% active).

3. Liquid alkaline cleaning composition according to claim 1, characterized in that, stabilizer / phase formation inhibiting agent is ammonium based cationic detergent active ingredient.
4. Liquid alkaline cleaning composition according to claim 1, characterized in that, said quaternary ammonium based cationic detergent active ingredient is benzyl-dimethyl-tridecyl-azanium chloride (100% active).

5. Liquid alkaline cleaning composition according to claim 1, characterized in that, said antioxidant and stabilizer is an organic acid, i.e. citric acid.

6. Liquid alkaline cleaning composition according to claim 1, characterized in that, said biodegradable detergent active ingredients are alcohol ethoxylate based C12-C14+6 EO and C12/18 - 10 EO n-butyl end-capped chain structures.

7. Liquid alkaline cleaning composition according to claim 1, characterized in that, in said composition the buffer and buffering agent is sodium chloride (100% active).

8. Liquid alkaline cleaning composition according to claim 1, characterized in that, formulation stabilizer is citric acid (100% active).

9. A production method of the liquid alkaline detergent being suitable for clean-in-place (CIP) utilization in the pharmaceutical, food, and cosmetics sectors, characterized in comprising the following process steps:

   in the approximately 90 wt% soft and/or demineralized water;
   - approximately 0.5 wt% nonionic surfactant C12-C14+6 EO alcohol ethoxylate based detergent active ingredient is dissolved,
   - after the completion of the dissolution, approximately 1.5 wt% nonionic surfactant C12/18 - 10 EO n-butyl end-capped chain alcohol ethoxylate is added and stirred until dissolved;
- approximately 2.5 wt% sodium hydroxide is added, stirred and dissolved;
- approximately 0.25 wt% sodium chloride is added and dissolved;
- approximately 0.8 wt% citric acid is added and dissolved;
- approximately 1.1 wt% of 50% quaternary ammonium compound solution is added and stirred until the turbidity of the solution is removed and volume of the solution is completed to 100% with water.

10. Production method of the liquid alkaline detergent according to claim 9, characterized in comprising the process step of adding and dissolving approximately 3 wt% sodium EDTA into said solution.

11. Production method of the liquid alkaline detergent according to claim 9, characterized in that, pH of said detergent solution is approximately 13.2.

12. A production method of the liquid acid detergent being suitable for clean-in-place (CIP) utilization in the pharmaceutical, food, and cosmetics sectors, characterized in comprising; the following process steps:
   in the approximately 90 wt% soft and/or demineralized water;
   - approximately 0.05 wt% nonionic surfactant C12-C14+6 EO alcohol ethoxylate based detergent active ingredient is dissolved,
   - after the completion of the dissolution, approximately 0.15 wt% nonionic surfactant C12/18 - 10 EO n-butyl end-capped chain alcohol ethoxylate is added and stirred until dissolved;
   - approximately 5 wt% citric acid is added and dissolved;
   - approximately 1 wt% sodium chloride is added and dissolved and volume of the solution is completed to 100% with water.
13. Production method of the liquid acid detergent according to claim 12, characterized in comprising: the process step of adding and dissolving approximately 0.2 wt% sodium EDTA into said solution.

14. Production method of the liquid acid detergent according to claim 12, characterized in that, pH of said detergent solution is less than 2.