SUMMARY

Basic drug pharmaceutical industries are assigned as red category as per Central Pollution Control Board categorization. Drug formulation industries are also pollution generating industries. Large industries are running effluent treatment plant (ETP) system to treat their own generated waste but small and medium size (SME) industries are reluctant about the waste minimization and waste treatment system implementation and development.

Present research comprises in-depth study of six pharmaceutical industries, those are, formulation industries as i) an industry producing large volume parenterals (LVP), ii) a formulation industry producing tablets and oral liquids, iii) a formulation industry implementing ISO 14001, International Standard, vi) a drug formulation company producing medicated ointments, and basic drug industries as v) a basic drug chloralkali industry producing sodium hydroxide and chlorine vi) isolation and identification of inoculums (named as *Pseudomonas aeruginosa* SSP1) present in the effluent of a basic drug manufacturing company in Kolkata producing Citric Acid, sodium citrate, sodium oxalate.

For large volume parenterals (LVP) production, raw materials used were Dextrose anhydrous, Sodium chloride, Sodium lactate, Calcium chloride, Potassium chloride, Sodium acetate, Sodium metabisulphate, Sodium sulphite, Dibasic Potassium phosphate, Magnesium Chloride, Ammonium chloride, Metronidazole Ciprofloxacin monolactate, Pefloxacin, Mannitol, Fructose, Glycerin, Tinidazole and the Water for Injection. In the pharmaceutical factory, LVP finished products and Water for injection failed to comply with the bacterial endotoxin limit of 0.5 EU/ml, specified by Indian Pharmacopea, 2010. Present researcher had fixed limit for all raw materials as 2.5 EU/gm and individual EU level of each input material had been determined. Thus knowing the total EU load before giving the batch charge, presently products were complying with the prescribed specifications.

Organic solvents (alcohol, methylene chloride and acetone) based film coating were used in oral medication like Metronidazole, Ofloxacin, Tinidazole tablets to prevent its release in stomach at acidic juice of pH 2-3, instead it would release in alkaline pH 7-9 at intestine. Organic solvent based coating solutions comprise hazardous chemicals which need to be changed by aqueous based coating solution. Change of organic based coating solution to aqueous based coating solution does not alter the medication, values of test parameters remaining within specification and effectiveness being ensured. Safety issues like personal protective equipments (PPE) were used by the concerned workers and the fume is not allowed to release to the atmosphere. Now due to above change, annually 12,000 litres of organic solvent and 80% of raw materials were saved. Moreover, due to use of aqueous solvent for coating, no safety issue arises.

A tablet formulation had been followed with a fixed formula for long period. Present investigator suggested reduction in the quantities of filler and binder based on certain important observations and some trial experiments. Care was taken to see that bioavailability of the products remain
same even after the change of formulation of paracetamol tablet as suggested. Dissolution test and assay test results show compliance with specifications before and after modification. Before modification dissolution was 86% and assay was 495 mg per average weight of tablets and after modification those are 89% and 498 mg per average weight of tablets respectively.

Tablet formulations of water sensitive materials were not done with starch paste; instead it was done with alcohol paste. Amoxicillin tablet has been prepared with alcohol paste. Present investigator has changed this alcohol paste system by slugging system. Slugging means direct compression of dry mixture of active and inactive ingredients to big size tablets, then breaking it to make granules and again compressing them in desired size tablets. So by this process use of hazardous organic solvents is discarded and thereby savings are achieved in all respects. Waste characteristics have been changed remarkably.

The industry producing oral liquids (viz. Paracetamol suspension made for pediatric use) under study uses sodium carboxy methyl cellulose, suspending agent and thickener, refined sugar or sucrose, sweetener and extra cleaning water. In the present study, the inactive materials quantity is reduced based on experience and some trial experiments, thereby saving materials and minimizing waste. Sodium carboxy methyl cellulose was reduced from 1.75 kg to 0.75 kg, refined sugar or sucrose was reduced from 120 kg to 80 kg, cleaning water from 300 litres to 200 litres. Assay of paracetamol suspension found before and after of the change remains within specification. Electricity consumption was reduced from 4.25 kWh to 3.00 kWh. Characteristic change in effluent generated from the pharmaceutical industry due to process modifications and reduction in quantity of raw materials may be narrated as follows: before modification Volume (m$^3$/h), pH, TSS (mg/l), TDS (mg/l), COD (mg/l), BOD (mg/l) are 05 – 10 m$^3$/hr, 5 – 9, 400-500, 600-700, 400 – 500, 200 – 250 respectively and after modifications those values are 03 – 7 m$^3$/h, 6.5 – 7.5, < 200, < 200, < 100, < 30 respectively and hence significant improvement in waste characteristics is achieved.

After adoption of Environment Management System, ISO: 14001 with regular self assessment / internal auditing for waste management in a pharmaceutical formulation industry, development of road map for cleaner production have been achieved. The water consumption has been reduced significantly. Powder spillage during sampling and weighing of raw materials (RM), contamination of air and land affecting human lungs, heavy sound generation during trolley movement carrying RM in production floor causing adverse effects on human ear, powder, broken pieces of tablets, torn strips, torn labels, torn papers on production floors, contamination of land, increasing load on effluent treatment plant (ETP), mixed waste generation after sweeping of floor in oral liquid department, oil leakage from trucks during transferring Light Diesel Oil (LDO) to boiler tank cause severe problem in the industry. To mitigate all these aspects, effective measures were undertaken and fruitful results are obtained. Characteristic change in effluent generated from the pharmaceutical industry due to ISO 14001:2004 implementation are as follows: before EMS implementation Volume (m$^3$/h), pH, TSS (mg/l), TDS (mg/l), COD (mg/l), BOD (mg/l) are 05–8 m$^3$/hr, 5 – 9, 500-600, 600-700, 500–600, 200–
300 respectively and after EMS implementation the values are 03–06 m³/h, 6.5 – 7.5, < 150, < 100, < 100, < 30 respectively and hence significant improvement is achieved.

One basic drug chloralkali industry is studied for waste minimization and waste treatment. The objective of the study is to emphasize on waste minimization in a basic drug plant producing sodium hydroxide and to find prospective measures to be undertaken to meet the need of proper environmental management. Corrective actions are taken to reduce wastage and to improve characteristics of wastewater by process modifications.

The following corrective measures are implemented as per suggestion. The equipments used for primary brine like settler, purifier are covered to prevent losses. Spent acids are sold to another industry to be reused further. The waste gas containing chlorine used to emanate during normal operation and that increases manifold during irregular plant operation and in emergencies.

Suggestion is forwarded to use weak caustic soda solution to absorb the same to produce sodium hypochlorite. Present investigator suggested providing suitable dosing of hydrogen peroxide and sodium bisulphate to neutralize and reduce chlorine content in wastewater.

The initial practice was to bring wastewater streams from stable bleaching powder and from aluminum chloride together and the pH of mixed wastewater would stand at 11-12. This was further neutralized with 26 liter of commercial hydrochloric acid daily. Similarly, wastewater stream from membrane plant and brine purification plant having low pH of 3-4 was neutralized with 32 kg soda ash daily.

Present researcher has altogether stopped acid/alkali consumption, instead all wastewater streams are suggested to mix in primary ETP for intermixing and automatic neutralization. He has suggested using the sludge generated in the treatment plant as fertilizer after composting, and also using it as a feed material in cement manufacturing, brick manufacturing and road construction. In ETP, quantity of soda ash consumed per annum before modification was 11,000 kg and hydrochloric acid was 9000 liter. After modifications consumption of both items turns nil.

Characteristic change in effluent generated from chlor-alkali industry due to process modification may be presented in the following manner: before modification Volume (m³/h), pH, TSS (mg/l), TDS (mg/l), COD (mg/l), BOD (mg/l), Mercury (mg/l), Chlorides (mg/l), Free Chlorine are 30–50 m³/h, 8 – 12, 2500, 7400, 250 – 300, 35 – 55,0.001, 4800, 1000 respectively and after modifications the values are 20 –40 m³/h, 7 – 9, < 1200, < 2000, < 200, < 35 ,0.001, < 1000, < 400 respectively, and hence significant improvements are achieved.

Measures are taken in Compressed Air network for reduction in pressure drop in the above basic drug industry. Pressure drop is a term used to characterize the reduction in air pressure from the compressor discharge to the actual point of use. Excessive pressure drop will result in poor system performance and excessive energy consumption. For prevention of pressure drop existing pipe lines are changed from 1.5 inch to 3 inches resulting in a reduction of pressure drop.
from 1 to 1.5 kg/cm². Compressor generation pressure reduced to 6 kg/cm². Energy savings per annum @ 300 days is Rs. 1.0 lakh/kW

One pharmaceutical basic drug industry has been studied for possibility of bioremediation of waste by microorganism Pseudomonas aeruginosa. From a basic drug manufacturing company in Kolkata producing Citric Acid, inoculums are collected from the outlet drain, cultured and a microorganism was isolated, identified as Pseudomonas aeruginosa named as Pseudomonas aeruginosa SSP1. It is understood that the organism Pseudomonas aeruginosa SSP1 grows by utilizing Citric Acid as a carbon source, so utilization activity of the strain on fifteen antibiotics and three non-antibiotics of Penicillin (Pc), Ampicillin (Ap), Piperacillin (Pp), Carbenicillin (Cb), Meropenem (Mp), Ceftazidime (Cd), Cefuroxime (Cr), Streptomycin (Sm), Gentamycin (Gm), Amikacin (Am), Azithromycin (Az), Norflox (Nf), Ciproflaxacin (Cf), Tetracycline (Tc), Chloramphenicol (Cm) at the concentration level of μg/ml are seen simultaneously with standard strain of Pseudomonas aeruginosa ATCC 27853. Utilization / degradation of Non Antibiotics Thioridazine (Tz), Chlorpromazine (Cpz), Methylglyoxal (Mg) in μg/ml is investigated by Pseudomonas aeruginosa SSP1, simultaneously with standard strain Pseudomonas aeruginosa ATCC 27853.

Above experiment shows that the isolated organism Pseudomonas aeruginosa SSP1 is resistant to Gm, Pc, Sm, Tc, Cm and Ap up to 5000 μg/ml, Mp, Tz, Cpz up to 2000 μg/ml, Cz, Cr, Cd, Mg up to 200 μg/ml, Az, Nf up to 100 μg/ml, Cf, Cb, Pp up to 50 μg/ml and sensitive to Ak at 25 μg/ml. So there is a scope for further study to ascertain the utilization pattern of the isolated organism with other drugs preferably non-antibiotics having antibacterial action and by the known strain ATCC 27853.

In a drug formulation company producing medicated ointments dosage forms, performance of ETP having screening, equalization, flocculation tank, sedimentation and membrane filtration system is studied extensively. It is observed that there is no flush mixing arrangement for mixing of coagulants and the cost involvement in membrane filtration is high. Study is aimed at improvement in the coagulation process by providing a flush mixer and reducing the cost of treatment by establishing a low cost treatment system.

Primary test results showed unsatisfactory values in the effluent of ETP as pH 5.7, TSS 520 mg/l, Oil & Grease 25 mg/l, BOD 370 mg/l, COD 1350 mg/l. A flash mixer for addition of coagulants and the low cost treatment system (Oxidation Pond) have been introduced by the present investigator and costly membrane filtration system was removed altogether. Test results after introduction of flash mixing of coagulants and oxidation pond in the ETP show improved values for pH (~ 7.1), TSS (~90 mg/l), Oil & Grease (~ 08 mg/l), BOD (~50 mg/l), COD (~300 mg/l).

Based on the findings of above total work done, it may be concluded that effective measures should be undertaken with regard to minimization and treatment of wastewater generated from
different pharmaceutical industries. At present some industries have adopted some of the measures but majority of industries in India are yet to adopt the effective measures. Extensive in-plant studies in the different industries are required to develop industry-specific waste minimization and treatment system.

Use of organic solvents like oxygenated and halogenated solvents is also increased in bulk drug industries and that need to be minimized.

There are plenty of scope for further research and study in pharmaceutical basic drug industries as well as formulation industries for waste reduction, waste minimization and wastewater treatment.