Waste Minimisation In The Bulk Pharmaceutical Industry

Presented in Part Fulfilment For the Degree of Master in Science in Environmental Protection

By
FINBARR FITZGERALD

Supervised By
DR. JAMES BRENNAN

Submitted To The National Council For Education Awards

June 1998

ACKNOWLEDGEMENTS

I wish to thank the following for helping me in the preparation of this thesis:-

Dr. James Brennan, my tutor, for his helpful comments and suggestions. Mr. Gerry Cahill of Pharmacia & Upjohn. Mr. Dermot Cunningham from the Clean Technology Centre, Cork. Mr. Gerard Rooney of SmithKline Beecham. Mr. Don Eglington of Pfizer Chemical Corp. Imelda Kelly for typing assistance.

Finbarr Fitzgerald

ABSTRACT

Waste disposal is a major problem for today's society. The traditional outlets for wastes, like landfilling are fast disappearing and for many types of wastes it is no longer an option. The problems of disposal of hazardous waste is even more problematical, especially with no established outlet in Ireland. The Bulk Pharmaceutical Industry. in Ireland is a major economic player but the industry has serious concerns about the availability of outlets for its hazardous and non-hazardous waste.

This has made the industry rethink its strategy to the management of waste. In the sixties and seventies, the emphasis was on end-of-pipe technology for the treatment of waste. In the late eighties / early nineties, the emphasis changed to waste minimisation. As a result, many of the Bulk Pharmaceutical plants developed a waste minimisation programme. A central element of the programme is the waste minimisation hierarchy.

Elimination ⇒ *Source Reduction* ⇒ *Recycling*

Treatment ⇒ *Disposal*

Establishing a waste minimisation programme in a plant will require the commitment of all employees from Senior Management to the Shop Floor Operatives. As with any project, best results can be achieved if the programme is well structured and organised -- in other words, if a system's approach is adopted. While the costs factor is very important and cannot be ignored, nevertheless to be consistent with the principle of sustainable development, it is important to consider projects which may be economically neutral. It is also important for the success of the programme to provide regular status reports on the state of progress.

Waste minimisation techniques can be broken down into four categories, namely inventory management, production process modifications, volume reduction and recovery. The first three categories can be classified under source reduction and the last one under recovery/reuse. In the Bulk Pharmaceutical Industry solvent recovery and reuse forms an important aspect of waste minimisation, but is limited to a certain extent by regulatory constraints. Process changes can also be complicated by the requirement for validation.

The practical application of waste minimisation is described in a case study of a Bulk Pharmaceutical. manufacturing plant located in the Cork area.

CONTENTS

WASTE MINIMISATION IN THE BULK PHARMACEUTICAL INDUSTRY

1.0 INTRODUCTION

The Environment has become one of the strategic issues facing industry in the 1990's. The message is clear: Industry must be proactive in finding effective, long-term solutions to problems that threaten the environment and our Health and Safety. This is not a simple task. Most companies find themselves coping with such issues as air and water quality, waste management, the need for sophisticated and expensive laboratory testing and monitoring, ecosystems management, the development of health and safety programs, remediation and construction and the need to comply with increasingly demanding governmental regulations.

Because of past incidents involving wastes a widespread public perception has grown that industrial wastes, especially from the chemical industry, are a continuing threat to health and the environment in Ireland. This is especially true in the Cork area where concerns have been voiced regarding emissions to atmosphere and to water. The chemical industry recognises these concerns exist, and is clearly aware of its responsibility to carry out its operations in a safe and efficient manner without harming its employees, the public and the environment. Although it makes good economic sense for companies to minimise the generation of waste, waste cannot be totally eliminated in the course of industrial activities.

In the past the various wastes arising from industrial processes tended to be looked at in isolation. Current thinking favours an integrated approach to pollution control. Integrated pollution control is a comprehensive approach to pollution abatement whereby the environmental impact of any development on all three media - land, air and water can be evaluated.

Waste minimisation can be regarded as an important element of sustainable development. The chemical industry has long recognised the importance of waste minimisation and has made considerable improvement in its efficiency. However, it is not complacent and is continuously increasing its effort towards better performance.

This report reviews the effort and progress of the bulk pharmaceutical industry in achieving waste minimisation. Also, in a case study, the programme of one particular bulk pharmaceutical plant is reviewed in detail. The report covers all wastes associated with the site, both hazardous and non-hazardous, energy and emissions to atmosphere.

2.0 THE BULK PHARMACEUTICAL INDUSTRY IN IRELAND

2.1 Characterisation

`The majority of the Bulk Pharmaceutical Plants were set up in Ireland in the early to mid seventies. The majority of the plants are located in the Dublin and Cork areas. The industry is dominated by Multi-National Companies with a very small indigenous Irish sector. Typical of the industry is low volume , high value output . The industry is a significant contributor to the Irish Economy. Estimated figures for 1995 were;

Employment;	16438 jobs attributable to the industry	
Economic;	Economic activity of over	IR£1.O Billion
	Capital Employed	IR£2.1 Billion

Nevertheless it has not been without its problems especially on its impact on the environment. According to Sheldon 25 to 100 pounds of waste are generated per pound of pharmaceutical product. To compound this problem a large proportion of this waste is often hazardous (usually solvent). In the past this was considered an acceptable price to pay for getting products to the market place. However in response to economic pressures and more stringent environmental regulations, Bulk Pharmaceutical Plants are now subjecting manufacturing processes to much closer scrutiny.

2.2 Impacts

<u>Air</u> Emissions of volatile organic carbons, NOx, SO2, and odour.

<u>Water</u> Wastes from Bulk pharmaceutical Plants can have very BOD loading.

<u>Wastes</u> Bulk pharmaceutical Plants produce a significant fraction of the total hazardous waste production Ireland. The initial

response of industry to minimise the environmental impact of its operations was to invest in end- of -pipe technology. The approach today is to adopt a combination of Integration Pollution Control, BATNEEC, and as a last resort , End- of - Pipe technology.

This is the Waste Minimisation Approach and can be described by the Waste Hierarchy.

(See Fig. 1)

Fig.1

WASTE HIERARCHY

GENERAL ELIMINATION
RAW MATERIALS/CHEMISTRY CHANGE

GENERAL REDUCTION
POINT OF SOURCE CONTAINMENT /
PROCESS CHANGE

RECYCLE
RECYCLE PURE STREAMS BACK INTO
PROCESS

REUSE AND RECOVERY
SOLVENT RECOVERY AND USED BACK
IN SAME/DIFFERENT PROCESS

TREATMENT
"END OF PIPE" SOLUTION INCINERATION
SCRUBBING / BIOLOGICAL EFFLUENT TR.

DISPOSAL
TO AIR / WATER / LAND

3.0 THE NATURE OF THE BULK PHARMACEUTICAL INDUSTRY

3.1 Introduction

The Bulk Pharmaceutical Industry is concerned with the manufacture of organic chemicals of varying complexity which are used as the active ingredients in pharmaceutical products. The product may be either the final dosage form which is shipped to the secondary manufacturers for incorporation into in tablets or capsules or be an intermediate stage product which is shipped for further processing.
The Primary production of bulk pharmaceuticals is normally a batch process with varying numbers of process steps. Some production cycles could have up to 20 steps. Many of the intermediate products are isolated and dried and act as the raw material for the next step. There is usually a yield loss at each step and this is the reason that the industry produces large volumes of waste relative to the quantity of finished product. For example an 80% yield for each stage of a 5 step synthesis results in almost 70% of raw materials going to waste. The problem is exasperated by the fact that the waste is often hazardous and difficult to dispose of. We will now take a tour through a typical Bulk Pharmaceutical manufacturing process and look at the materials used, the unit operations employed and the resulting outputs. Figure 2 gives a schematic of the overall processes.

3.2 Raw Materials

3.2.1 Starting Materials (Pre-Cursors)

These are the basic building blocks of the desired end molecule and often are the basic skeleton of the active ingredient to which are attached various active groups to impart the desired activity to the product. They are often highly toxic and of high value and for this reason they do not normally constitute a waste problem.

3.2.2 Solvents

Solvents are utilised both as a reaction medium and for purification . Table 1 lists typical solvents employed in the Bulk Pharmaceutical Industry.

Organic solvents constitute the greatest proportion of hazardous waste produced by the Bulk Pharmaceutical Industry and indeed of the hazardous waste produced nationally.

3.2.3 Reagents

These are employed as reactants themselves or in some way to influence , the speed and direction of a reaction, to neutralise impurities or influence solubility or precipitation. Table 2 lists some typical reagents employed in the manufacture of bulk pharmaceuticals.

3.2.4 Ancillary Chemicals

These are materials which are not directly involved in the reaction process but are utilised for process control. Examples are Brine (Methanol\Water), Glycol and Chilled Water for cooling purposes , Steam for heating, Nitrogen and Carbon Dioxide for inertion and transfers Activated Carbon, Ionexchange Resin and Filter Aid for filtration and purification.

3.2.5 Maintenance Chemicals

These are usually associated with the ancillary services, for example Freon for low temperature coolant, Lubricating oils, Thermic fluids as heating medium, boiler water treatment chemicals, cooling tower water treatment chemicals, chemicals associated with the waste water treatment plant, scrubbing liquors, filter aids and activated carbon.

TABLE 1

Ethanol
Methanol
Isopropanol
n-Butanol
Acetone
Methylethyl Ketone
Methyl Isobutyl Ketone
Di Isopropyl Ether
Petroleum Ether
Diethyl Ether
Ethyl Acetate
n. Hexane
Cyclohexane
Di Chloromethane
Di Chloroethane
Triethanolamine
Toluene
Tetrahydrofuran
Xylene
Acetonitrile
Carbon Disulphide
Chloroform
Acetic Acid
Pyridine
Dimethyloformamide
1, 4 Dioxane

TABLE 2

Reagents

Triethylamine
Dimethylsulphate
Lithium Aluminium Hydride
Grignard Reagent
Sodium Methoxide
Potassium ter Butoxide
Sodium Metal
Potassium Metal
Zinc Dust
Steroids
Hydrogen Chloride
Hydrogen Bromide
Chlorine
Bromine
Hydrogen
Phosgene
Phosphorous Oxychloride
Chloracetyl Chloride
Ammonia

3.2.6 Packaging Materials

These include such items as plastic liners, fibre and plastic drums, pallets etc..

3.3 The Process

3.3.1 Dispensing

Many of the reactions to produce the bulk pharmaceutical active are stoichiometric in nature so it is important that the starting materials are accurately weighed out and dispensed. This operation takes place in a dedicated section of the plant and the materials are weighed into containers which are suitable for making additions to reactors. These containers range from an IBC (intermediate bulk container) of 1000L capacity to Mueller Drums of 200L capacity to containers for high containment e.g. La Calhene units of 10L capacity.

3.3.2 Reaction

The basic chemical reaction or synthesis is carried out in a reactor This is the heart of the bulk manufacturing process. Reactors are agitated vessels and can range in size from 100 to 10,000 L. They are often glass lined because of the aggressive nature of the materials used in the process. Typical reactions which may be carried out in a reactor are, alkylation, sulphonation, esterification, substitution, condensation, reduction, etc.

Solid materials are charged through the manlid or as is more common today through some type of high containment system like a glovebox or a La Calhene system. Liquid solvents and reagents are piped in via a manifold system. The chemical reaction takes place under varying conditions of pressure and temperature and may be very fast (mins.) or may take several hours or even days. Reactors are equipped with an agitator to promote mixing of the ingredients to ensure a uniform reaction mixture and to promote a uniform temperature of the reactor contents.

Reactors are equipped with some means of heating\cooling the vessel contents. What is typically employed is a jacket through which flows a "Thermic" fluid which is heated or cooled by means of an heat exchanger. Temperatures typically range from -30 to +120 degrees centigrade. Also associated with the reactor are head tanks for liquid charging to the reactor, distillate receiver vessel and a vent or reflux condenser. The reactor has a number of inlet and outlet lines for the entry or removal of gases, liquids or solids.

3.3.3 Liquid-Liquid Extraction

This unit operation relies on the unequal distribution of components between two immiscible liquids . Generally the liquid solution (feed) is contacted intimately with a suitable incompletely miscible liquid (solvent) which preferentially extracts one or more components. This results in a solvent lean residual feed solution with one or more components removed (raffinate) and a solvent rich solution containing the extracted solute(s) (extract).

3.3.4 Crystallisation

After reaction the product of interest is usually dissolved in the solvent medium. To separate the product from the mother liquor it is crystallised in a vessel called a crystalliser. This vessel is very similar to a reactor and indeed a reactor is often used for this purpose. Crystallisation is carried out either by cooling the mother liquor or by evaporating the solvent to the supersaturation point.

3.3.5 Solids Separation

After crystallisation the solids have to be separated from the mother liquor. This can be carried out in one of three ways:

* By Filtration
  The slurry is passed through a filter medium and the product is retained on the filter cloth. In the Bulk Pharmaceutical Industry this technique is employed only for small batches.

* By Centrifugation
  This is by far the most common technique where the slurry is spun at high speed and the crystals are retained on a filter medium. This system may be either continuous or on a batch basis.

* Filter/Dryer
  This is a combination of a filter and a dryer. While a filter/dryer is expensive it is becoming more popular because it affords a high degree of containment and is suitable for potent materials.

3.3.6 Drying

After centrifugation or filtering the product is usually about 25% solvent wet, and must be dried to remove this solvent. Drying is often a complicated process in the Bulk Pharmaceutical Industry, partly because of the temperature sensitivity of the product and partly because of the danger of contamination from the material of construction of the dryer. The two main techniques are tray drying or vacuum agitated drying.

In tray drying the product is spread out evenly on trays and dried in a steam or electrically heated oven. The drying is normally carried out at atmospheric pressure but it can also be carried out under vacuum. Vacuum dryers are usually cone shaped with an auger for agitating the product. They are usually heated with hot water and operate under high vacuum. For both types of dryers the evaporated solvent is passed to some form of abatement system.

3.3.7 Milling and Sieving

This unit operation is carried out to break up lumps that may have formed from the drying process, to blend the product and to screen out foreign matter (e.g. metals) which may have inadvertently entered the product.

3.3.8 Abatement, Treatment, and Recovery Systems

Condensers

Condensation is used as a primary gaseous emission abatement system. Its use and location is aimed at reducing raw material losses, increasing recovery potential and reducing emissions of volatile components in gaseous emissions. The cooling services available can range from +6 (cooling tower water) to -70 (liquid nitrogen) degrees centigrade. Condensate will be routed to one of the following destinations depending on process requirements.

(i) Returned to the source vessel
(ii) Collected and returned to the process
(iii) Collected for recovery, treatment and/or disposal as appropriate.

Scrubbing

The main types of scrubbers employed in the Bulk Pharmaceutical Industry are either the packed column or spray type. The packed column types are employed for gaseous emissions and the spray type for particulates. The abatement mechanism is absorption or chemical reaction or both. The scrubbing liquor may be :

- Water for polar compounds
- Hydrocarbon Oil for non-polar compounds
- Sodium Hypochlorite where oxidation is required
- Caustic Liquor for acid gasses
- Sulphuric Acid for ammonia and amines

Filtration

Gaseous streams and extraction systems are fitted with filtration systems to remove dirty particles prior to discharge to atmosphere. These filters are often of very high efficiency and capable of removing 99.99% of particulates with a particle size down to 0.12 microns.

Carbon Adsorption

This is the process where gaseous Volatile Organic Carbon molecules are adsorbed onto the surface of activated carbon in the form of regenerable carbon beds. When the beds become saturated they are regenerated by passing steam through them which strips off the adsorbed solvent. Hot nitrogen is sometimes employed instead of steam and it has the advantage of reducing the volume of regeneration liquor. It is of course more expensive than steam. Activated carbon is also employed in the form of non-regenerable cartridges or drums to reduce emissions of volatile organic carbons at specific points prior to release to atmosphere.

Thermal Oxidation

This is a relatively new technology and involves the vapour phase oxidation of the volatile organic carbon by passing it through a hot bed of granular material, for example, sand. They operate at typically around 800 degrees centigrade and are most suitable for non-chlorinated solvents. This technology is now also being developed for volatile chlorinated solvents.

Incineration

Six of the Bulk Pharmaceutical Plants in Ireland utilise incineration for the abatement of volatile organic carbon and for the disposal of waste streams. Incinerators can be designed to burn gases, liquids or solids and typically operate at between 1000 to 1200 degrees centigrade with a residence time of 1 to 2 seconds. The installation of incinerators is subject to much controversy and in some instances outright opposition because of the fears of dioxin formation especially if chlorinated solvents are being incinerated.

Wastewater Treatment

For aqueous streams contaminated with biodegradable organics biological wastewater treatment is employed. The most common technique employed by the Bulk Pharmaceutical Industry is aerobic treatment although there are a few instances of anaerobic treatment. In either case the purpose is to biologically oxidise the waste prior to discharge and thus prevent oxygen depletion in the receiving water.

Stripping

This technique is employed to strip traces chlorinated or non-biodegradable solvents from aqueous waste streams prior to discharge to the wastewater treatment plant or to sewer. This may be carried out by air stripping or by steam stripping (distillation).

Distillation

Solvent recovery by distillation is employed within the constraints of producing high purity pharmaceuticals for human health care. The function of solvent recovery is to re-use solvents in the processes in which they were generated as waste streams. Recovered solvent cannot be used in the final isolation step.

3.4 Waste Arisings

Wastes can arise from a number of locations / operations in the plant and can be broadly categorised under the following headlines:

- Raw Materials Storage
- Production Processes
- Abatement Systems
- Utilities

3.4.1 Raw Materials / Storage

Wastes can arise from off-spec. material, out-of-date materials, packaging materials, e.g., containers, bags, liners, pallets. Packaging materials are often contaminated with hazardous residues and have to be treated as hazardous waste. Also decontamination of metal containers can generate both hazardous and non-hazardous waste. From the tank farm operations, waste can arise from inadvertent spills, tank overflows, transfer hose emptying, tank cleaning, tank bottoms, bund water.

3.4.2 Production Processes

The bulk of the waste generated by the Bulk Pharmaceutical Industry arises from the Production Process:

- Mother Liquors
- Vessel and Line Washings
- Solvent and Aqueous Phase Splits
- Distillates
- Gaseous and Particulate Emissions
- Filters and Filter Residues
- Still Bottoms
- Aqueous, waste streams slightly contaminated with solvent, e.g., from washes, vacuum pump water
- Off-spec Material, e.g., reject batches
- Filter, cartridges and contaminated protective clothing
- Contaminated plant and equipment

3.4.3 Abatement Systems

The wastes arising from abatement systems include:

- Sludges from the Waste Water Treatment Plant
- Liquor from the regeneration of activated carbon beds
- Activated carbon drums and cartridges
- Scrubber liquors
- Dust and particulate filter cloths
- Also from incineration

3.4.4 Utilities

The waste arising from utilities include:

- Waste oils
- Waste cooling fluid, e.g., brine or glycol
- Loss of CFC from cooling systems
- Boiler blow-down (leading to loss of boiler water treatment chemicals)
- Cooling tower water
- Regeneration water from ion exchange units
- Decontamination of the purified water system.

4.0 ELEMENTS OF A WASTE MINIMISATION PROGRAMME

4.1 Introduction

Waste minimisation involves any technique , process or activity which either avoids , eliminates or reduces a waste at its source , usually within the confines of the production unit, or allows reuse or recoiling of the waste for benign purposes. Synonymous terms include:

* waste minimisation
* waste reduction
* clean technologies/clean engineering/clean processing
* pollution prevention/reduction
* environmental technologies
* low and non- waste technologies

While emphasis is placed on the word 'waste', it is important to note that all emissions of materials into air, water and land, as well as energy consumption, should be considered in a waste minimisation programme.

4.2 Management/Policy

There should be a clear policy commitment to waste minimisation. Objectives should be defined and a strategy for their achievement should be set out.

In order to succeed with waste minimisation, the commitment, participation and support of top management is an essential starting point. Long term waste minimisation plans should be integrated into business strategies to reflect investment and profitability implications, thus making business managers jointly accountable for waste minimisation results.

The training and motivation of all employees is vital to the success of a waste minimisation programme. It is their skills and attitude which will determine the rate and extent of progress. Perhaps the greatest challenge is to overcome preconceived ideas and inertia and generate a waste reduction culture with a willingness to challenge conventional thinking.

4.3 Hierarchy

The hierarchy of waste management practices is detailed in Table 3. As noted earlier the common approach to dealing with waste has been to treat and dispose (end-of-pipe approach) i.e. the bottom rung of the waste hierarchy ladder. Waste minimisation is concerned with the first, second, and third levels of the hierarchy, i.e. elimination, source reduction and recycling. The most preferred is elimination but in practice this is not always feasible.
It is important to note that waste minimisation is not, in most cases, concerned with;

* Action taken to treat the waste after it has been generated e.g. incineration, scrubbing, biological treatment.
* Dilution of waste to reduce its toxicity or to satisfy regulatory permits.
* Transferring waste from one environmental compartment to another, e.g. the treatment aqueous wastes to generate a sludge for landfill. Exceptions to above would be heat recovery from incineration or the utilisation of bioplant sludge as compost.

It is important to note here that we are ultimately concerned with minimising the impact of waste on the environment. This may involve the substitution of a hazardous material with a less hazardous one but with no reduction in the quantity generated.

4.4 **Methodology** (See Fig. 3)

4.4.1 Management Commitment

For any waste minimisation programme to succeed it has to have the backing of senior management. They will set objectives and targets and generally give effect to the waste minimisation aspiration outlined in the company's environmental policy. It is a good idea if a senior manager is assigned to the programme. Also some of the waste minimisation programs may require capital investment which would require the sanction of senior management. While programs with an economic pay-back are generally assured of support , programs which are economically neutral are deserving of support and must be promoted to be consistent with the principle of sustainable development.

4.4.2 Assessment

The Waste Minimisation Team

Waste minimisation assessment and evaluation will effect all the functional groups in a company. It is important therefore that the team is drawn from these functional groups (production, engineering, quality assurance, finance, purchasing) and should represent specific knowledge areas. The team can be drawn from all levels within the company organisation from production operators to senior management. It would be desirable that the team leader would be a senior manager and he would act as overall co-ordinator and "champion" of the waste minimisation programme.
The programme will have a much greater chance of success if employees are given a sense of ownership and are encouraged to ;

* Help define company goals and objectives
* Recommend ways to eliminate or reduce waste at source
* Design or modify forms and records to monitor materials used and waste generated.

In order to act as a catalyst and to counter pre-conceived ideas held by plant personnel, it may be a good idea to include at least one team member from outside the company. This external member could be either a corporate representative or a consultant with waste minimisation expertise.

(a) Goals And Timescales

The first step in a waste minimisation programme is to set realistic goals and timescales, that are consistent with the companies environmental policy.

Goals should be:

* Well defined
* Meaningful to all employees.
* Challenging yet achievable
* Flexible.

Examples might be:

* Eliminate the use of class 1 solvents in the process by the year 1999.
* Reduce the overall quantity of waste sent to landfill by 50% over the next five years. The goal setting process will involve the waste minimisation team in conjunction with Senior management.

(b) Data Collection

The planning of a waste minimisation programme should be based on an accurate knowledge of the quantity, composition and characteristics of waste streams from all production units and related material handling operations. Much of the data needed for the assessment phase may be available as part of normal plant operations or in response to existing regulatory requirements. As a first pass assessment the following should be carried out:

* Identify all waste streams and emissions generated on site
* Identify all losses,(including energy), to air, water and land.
* As far as possible quantify waste streams. This will highlight areas where more detailed information is required.

* Conduct a preliminary assessment of reduction opportunities and barriers to implementation.

The above exercise should highlight the significant wastes generators and provide a focus for a more detailed assessment. Also at this stage some wastes minimisation opportunities may become apparent.
Following from the above a more detailed assessment should be carried out. The following sources for facility information should be available:

Process Information.

* Process Flow Diagrams. (PFD'S)
* Piping and Instrumentation Diagrams. (P&IDs)
* Block Flow Diagrams. (BFDs)
* Drug Master Files. (DMF)
* Operating Manuals.
* Equipment Lists.
* Equipment specifications and data sheets.
* Plot Plans and General Arrangement Drawings.
* Batch Records

Regulatory Information

* Waste Shipment Information.
* Emission Inventories.
* Annual Environmental Reports.
* Environmental Audit Reports.
* Permits and Permit Applications.
* Spill/Release Reports.
* Spill and Leak Containment and Countermeasure Plans.

Raw material/Production Information.

* Product Composition.
* Material Safety Data Sheets.
* Product and Raw Material Inventory Records.

* Production Schedules.
* Batch Record Books.

Economic Information.

* Waste Treatment and Disposal costs.
* Product, Utility, and Raw Material Costs.
* Operating and Maintenance Labour Costs.

Other Information.

* Environmental Policy Statements.
* Standard Operating Procedures.
* Standard Costs for each Product.

Evaluation of this data will provide a more accurate estimation of the wastes generated on site and associated costs. For process materials the generation of an overall Mass Balance may be useful at this stage. Such a balance is an organised system of accounting for the flow, generation, consumption and accumulation of materials in a process. In its simplest form, a mass balance is drawn up according to the mass conservation principle:

Mass In = Mass Out - Generation + Consumption + Accumulation

If no chemical reactions occur and the process progresses in a steady state, the material balance for any specific compound or constituent is as follows:

Mass out = Mass in

Drawing up a process flow diagram (Fig. 4) will help in the generation of a mass balance. The mass balance will help to identify "information gaps" and indicate where further analysis may be required to quantify material losses. Ideally all waste streams and plant operations should be assessed. However it is advisable to prioritise the options to match the available manpower and resources and to achieve some early success. If it is tried to cover too many options the team will become overwhelmed and the project will not succeed.

Factors to be taken into account when prioritising options include:

* Compliance with current and pending legislation.
* Cost of waste treatment and disposal.
* Potential environmental and safety liability.
* Quantities and hazardous properties of the waste.
* Potential recovery of valuable by-products.
* Reducing energy use.
* Safety hazards to employees and the general public.
* Security of material supply.
* Security of waste disposal route.
* Minimising water usage.
* Achieving early success.

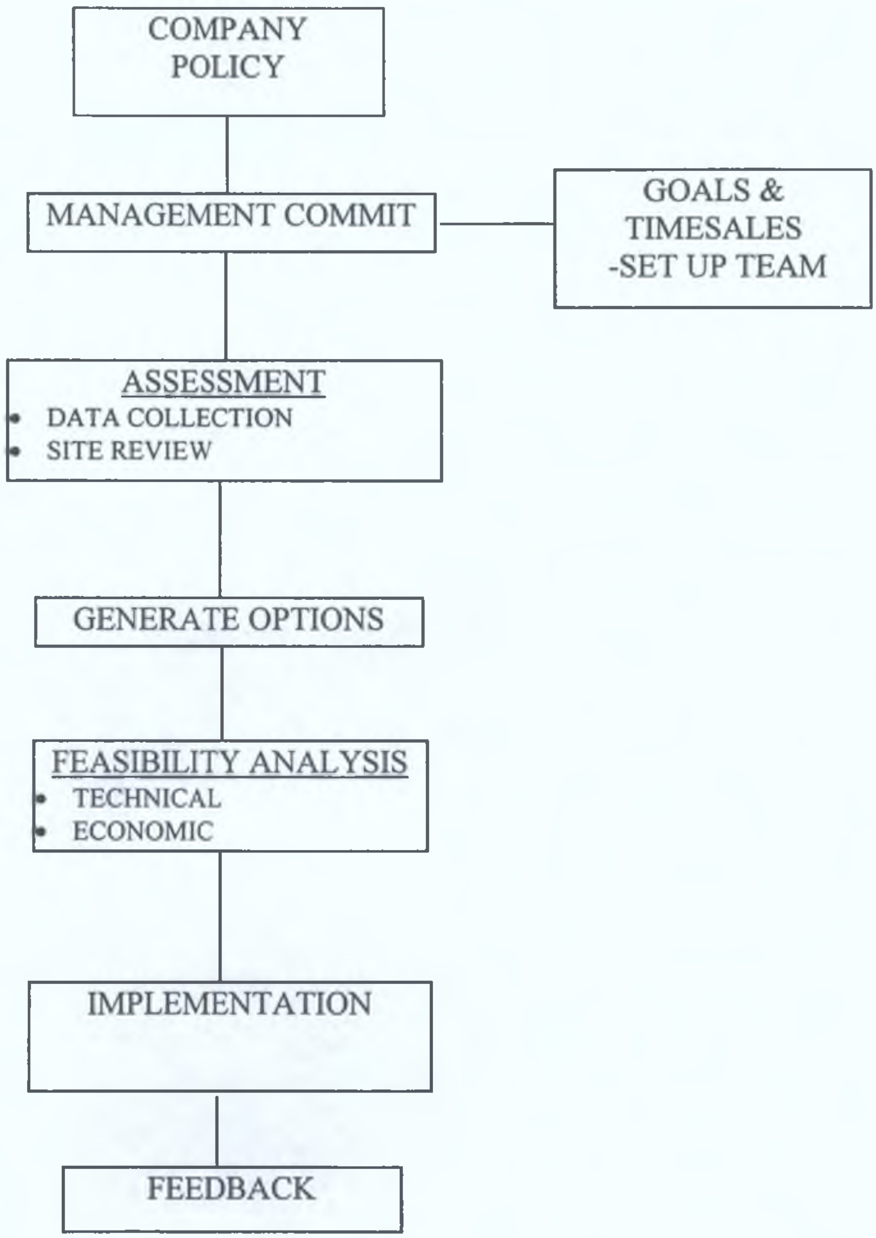
(c) Site Review

Having gathered the necessary information and prioritised the waste minimisation options it is then advisable to review the process on site. Specific guidelines for the site review include the following :

* Organise assessment team and issue an agenda in advance ; relevant personnel in the area being studied should be provided with the agenda in advance of the site inspection.
* Schedule the inspection to coincide with operations specially related to waste generation (e.g. start-up, shut-down, product change, reactor charging, vessel cleaning, boil ups, transfers etc.)
* Monitor the operation at different times during the shift, and if necessary, during several shifts, especially when waste generation is highly dependent on human involvement. (e.g. in cleaning operations, nitrogen transfers, rinsing etc.)
* Interview the operators, shift supervisors, and chargehands in the area under review. Discuss the waste generation aspects of the operation with them.They can be a very important source of information on the generation and sources of waste streams and can provide ideas for their minimisation.
* Observe the housekeeping; checks should be made for spills and leaks, odours and fumes, and an assessment

Figure 3

WASTE MINIMISATION METHODOLOGY

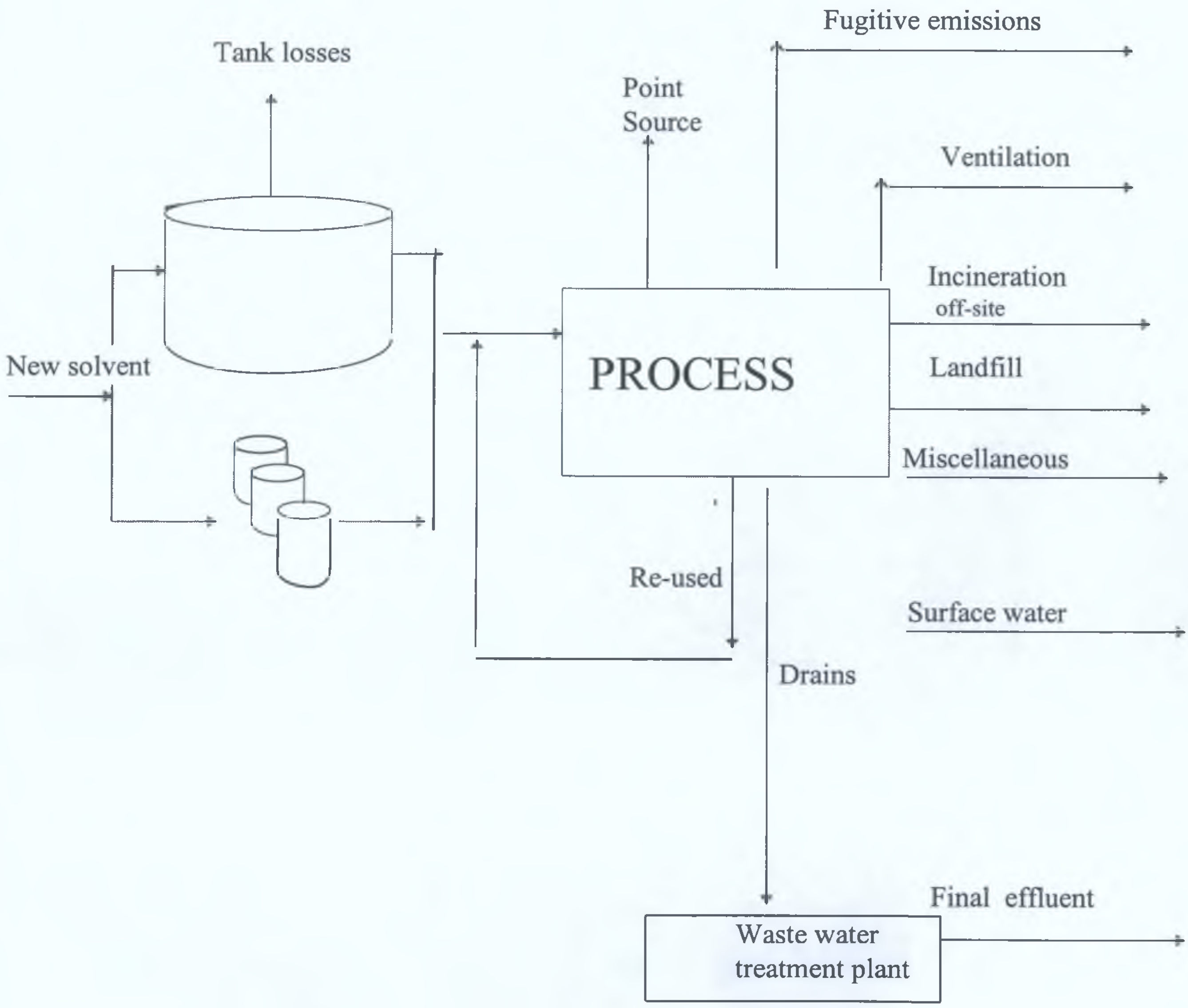


Hierarchy of Waste Management Practices

Elimination	Complete elimination of waste	↑
Source Reduction	The avoidance, reduction or elimination of waste, generally within the confines of the production unit, through changes in industrial processes or procedures	Highest Priority
Recycling	The use, reuse and recycling of wastes for the original or some other purpose such as input material, materials recovery or energy production	
Treatment	The destruction, detoxificiation, neutralisation, etc., of wastes into less harmful substances	
Disposal	The discharge of wastes to air, water or land in properly controlled or safe ways such that compliance is achieved; secure land disposal may involve volume reduction, encapsulation, leachate containment and monitoring techniques.	Lowest Priority ↓

Table 3

Fig. 4 Process Flow Diagram



should be made of overall site cleanliness. Other important areas are leaking valves (a visit to the workshop may be beneficial to establish the leak history of equipment), water hoses left running, nitrogen left on after transfer has been complete.

* Investigate the process from the point where raw materials enter the area to the point where products and wastes leave the area. Again as mentioned previously a process flow diagram will help in forming a picture of the area and identifying all the inputs and outputs.
* Identify all suspected sources of wastes.

The inspection should result in the formation of preliminary conclusion about the causes of waste generation. Confirmation of the preliminary conclusions may require;

* additional data collection
* additional data analysis
* further site visits

The origin and causes of waste generation should now be understood and sufficient information is available to generate wastes minimisation options.

4.4.3 Generation Wastes Minimisation Options.

The next step is to generate a comprehensive set of waste minimisation options for subsequent technical and economical evaluation. The objective is to place wastes minimisation options into priority groups in order to guide the allocation of resources for detailed feasibility analysis.

The process for identifying options will follow the waste minimisation hierarchy as shown below:

Reduction at Source	
Recycle/Reuse	↑ Order
Treatment	of
Disposal	Preference

* Source reduction techniques are considered to be good operating practices since they avoid or minimise the generation of waste. Thus options which fall into this

category should be placed in the highest priority group.
* Recycling techniques, either on-site or off-site, allow waste materials to be put to a beneficial use However, since recycling techniques do not avoid the generation of waste, they should not be ranked alongside source reduction techniques.
* Treatment options should be considered only if acceptable source reduction and recycling options cannot be identified.

The screening procedure therefore will eliminate options that appear impractical, inferior or otherwise of marginal value.

The process by which waste minimisation options are identified will occur in an environment that encourages creativity and independent thinking by the members of the assessment team. Brainstorming sessions with the team members are effective in generating options. The actual screening process can be carried out by an informal review and a decision made by the team leader. For each option the following should be considered:
* What is the main benefit to be gained ? - economic, regulatory, liability, safety etc.
* Does the necessary technology exist to implement the option ?
* Will regulatory approval be required?
* Can the option be implemented without major disruption to the production schedule?

The ranking process should take into account the ease with which an option can be implemented. Some options, for example, those which are considered to be good housekeeping, may require only procedural changes and incur no capital investment. Implementation could therefore be quick and not require further evaluation if potential cost savings have been identified.

4.4.4 Feasibility Analysis

The previous exercise will have developed a list of prioritised options for waste minimisation. These options should now be examined to determine which are technically and economically feasible for implementation. Options that are considered impractical, marginal or economically non-viable are not considered for further evaluation. Depending on the resources currently available, it may be necessary to postpone feasibility assessments for some options. However, all options should be evaluated eventually.

The technical evaluation determines whether a proposed waste minimisation option will work in a specific application. Technical evaluation criteria include the following:

* Has safety been compromised?
* Will product quality be maintained?
* Dose the necessary technology exist to develop the option?
* What are the main benefits to be gained by implementing this option. (e.g. financial, compliance, liability, workplace safety, etc.)
* Is additional labour required?
* Are the necessary utilities available, or must they be installed, thereby further raising the capital investment required.
* How long will production be disrupted to install the system.
* Is special expertise required to operate or maintain the new system.
* Do the system create other environmental problems.

All departments in the plant that will be affected directly if the option is adopted should be party to the technical evaluation. If, after evaluation the project appears unfeasible or impractical, it should be dropped.

Waste minimisation projects are subject to the usual economic criteria as all other proposed projects. However, it must be emphasised, that the true cost of waste generation may be difficult to determine by the usual accounting practices. Companies should take a wider and more long term view of the cost of wastes and incorporate the principle of sustainable development in their deliberations. A simple cost/benefit analysis may mitigate against many worthwhile projects and certainly economically neutral projects should be considered. Obviously projects with a cost benefit will be promoted and the following costs criteria should be evaluated:

* Regulatory costs
* Raw material costs
* Site management costs related to storage, tracking and shipping of wastes.
* Disposal costs
* Potential liability costs associated with improper disposal
* Treatment costs
* Capital costs

Projects with a significant capital costs will require a more detailed analysis. Attempting to determine the true management costs associated with generating wastes at a particular plant will give managers the opportunity to truly realise waste management costs and waste minimisation will become more attractive.

4.4.5 Implementation

Waste minimisation projects that only involve operational, procedural or material changes i.e. without additions or modifications to process and to equipment should be implemented as soon as the potential costs have been determined. The Bulk Pharmaceutical Industry has to be careful as regards changes to materials and processes. Depending on the step, the change may require approval by the F.D.A. or other regulatory bodies. This can be an expensive and long drawn out procedure with no guarantee of success at the end of the project. As a general guide any change that will affect the "Batch Record Book" or the "Drug Master File" will require the approval of the F.D.A. Projects that require the installation of equipment will follow the usual procedure for any other plant improvement project i.e.:

* Justify project and obtain funding
* Installation
* Implementation
* Evaluate performance

If a project appears to be potentially very profitable but cannot be exploited until either a new technology is commercially available or major operational changes are required, then help may be sought from external bodies which include:

Department of the Environment
European Union
Clean Technology Centre (C.T.C.)

4.4.6 Monitoring And Reporting Of Progress

A useful measure of the effectiveness of a waste minimisation project is its payback. For some projects this may be relatively simple e.g. savings in raw material costs, reduced waste disposal costs, reduced energy costs, etc. Highlighting these cost savings gives a powerful incentive to senior management to continue to support waste minimisation projects. However, one has to be careful that costs are just not transferred from one cost centre to another, e.g. reducing solvent incineration costs by diverting the stream to the wastewater treatment plant and thereby increasing the costs of sludge disposal. The costs have to be related, in some way, to the costs of producing the product. Also the cost savings may not be very tangible e.g. reduced liability, workers safety, etc. Nevertheless costs and profitability are powerful factors and cannot be ignored.

An obvious waste minimisation parameter is actual reduction in the quantity of waste generated, the units of energy consumed or the number of gallons of water consumed. Again as for the payback described above, it is not as straightforward as it seems and the following criteria should apply:

* the quantity must be measurable, data may come from a variety sources
* measuring techniques may not be available for all waste streams :this is especially true with fugitive emissions which are particularly difficult to measure
* Regulatory changes may appear to change quantities of wastes
* The waste minimisation project may have shifted the waste material:

  - to another plant stream
  - to another environmental medium
  - into the product

Some materials will be quite easy to monitor and measure e.g. electricity usage, gas consumption, water usage. Other materials e.g. solvents can be quite difficult to monitor. The most effective approach here is to carry out a material mass balance for the substance in question. This involves tracking the quantities of materials flowing into and out of the facility. It uses data on the quantities of materials purchased, produced and destroyed in the production, and incorporated in products and by-products, as well as discharges to waste treatment and disposal.

In plants where production rates may change from year to year, new products may be introduced and old ones dropped, it is necessary to standardise or normalise the measures used to track progress. Possible normalising factors include:

* hours of process operation
* hours of employee work
* weight of product produced
* mix of products produced

* number of batches processed
* new products introduced
* discontinued products

The Irish E.P.A. propose a system of indices for measuring waste reduction. One index is called the index of gross eco-efficiency (IGEE) and is defined as the proportion of gross process waste to gross usage.

$$IGEE = \frac{\text{gross process waste}}{\text{gross usage}} \times 100$$

Gross usage is defined as the total usage of a given material in a product line and includes new raw materials as well as raw materials arising from on-site recovery from process emissions. Gross process waste is defined as the amount of waste that is emitted from the process via air, effluent and waste emissions. It dose not include materials incorporated into the product and is gross of any amount recovered.
Another useful index is the Nett Eco-Efficiency index.
This is defined as the proportion of Nett Process Waste to Gross Usage,

$$INEE = \frac{\text{Nett Process Waste}}{\text{Gross Usage}} \times 100$$

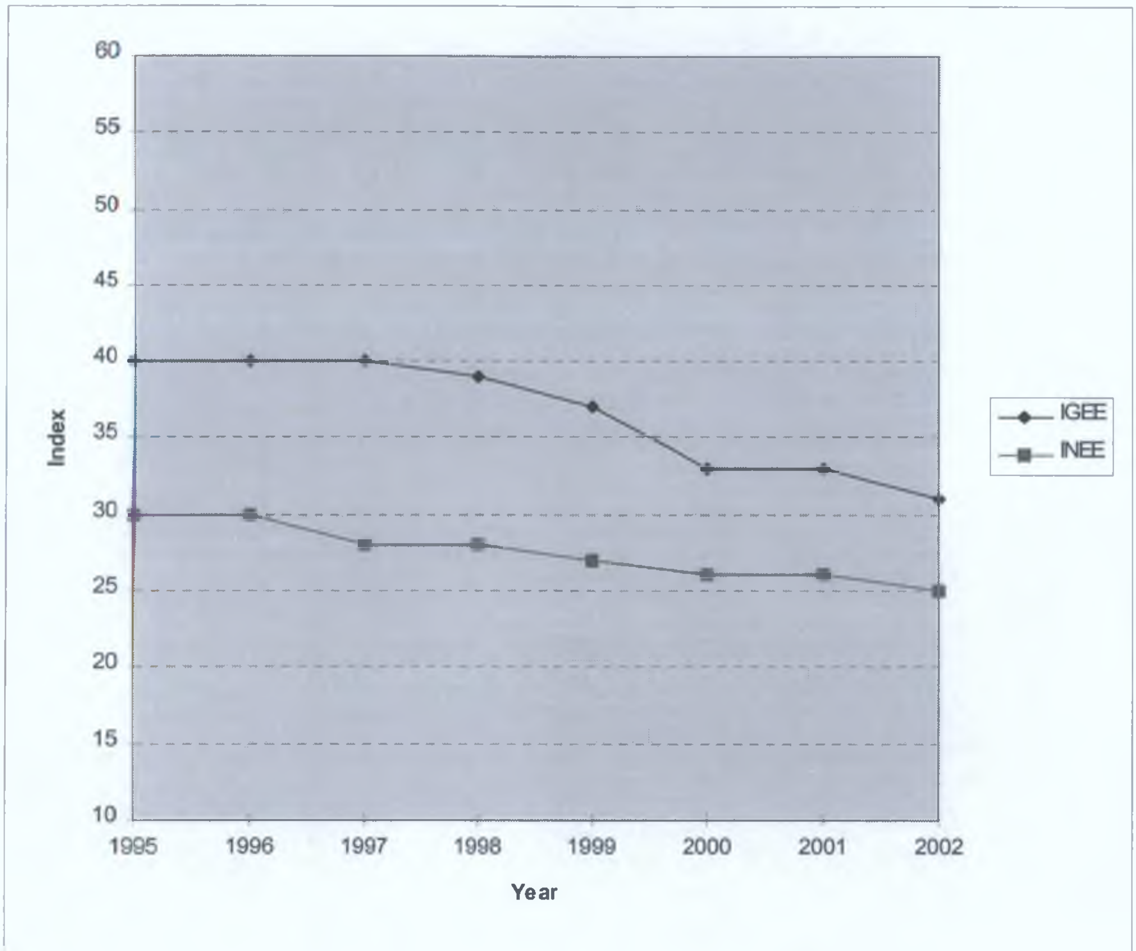
$$= \frac{\text{Gross Process Waste-Material Recovered}}{\text{Gross Usage}} \times 100$$

Nett Process Waste is defined as the amount of waste that is emitted from the process minus the amount that waste that is recovered on or off-site.
Gross and Nett Eco-efficiency Indices are very useful trending tools. They may be plotted from year to year and any improvements in waste generation/recovery etc. may be easily seen. Fig. 5 is an example of such a trend graph.

The toxicity of the wastes should be looked at, not just the quantity produced. This is especially true for hazardous waste. For example the substitution of a toxic substance with a less toxic substance may involve no change in the quantity of waste arisings, indeed in some cases it may increase, but nevertheless, the substitution will have a positive environmental impact. Hence a measure of toxicity may be appropriate. There are standard methods for measuring environmental toxicity of waste streams e.g. L.C.50 Daphnia, Algae Toxicity, etc.

Finally it is very important that progress or the lack of it, is reported widely in the company. This is vital to maintain the momentum of the program and to publicise success stories. It should be done on a regular basis preferably by posting charts and graphs on the notice board. It is important to remember that waste minimisation is as much a "state of mind" or culture as about process engineering. Fig. 6 is an example of a chart that might be posted.

Fig. 5 IGEE & INEE for Toluene



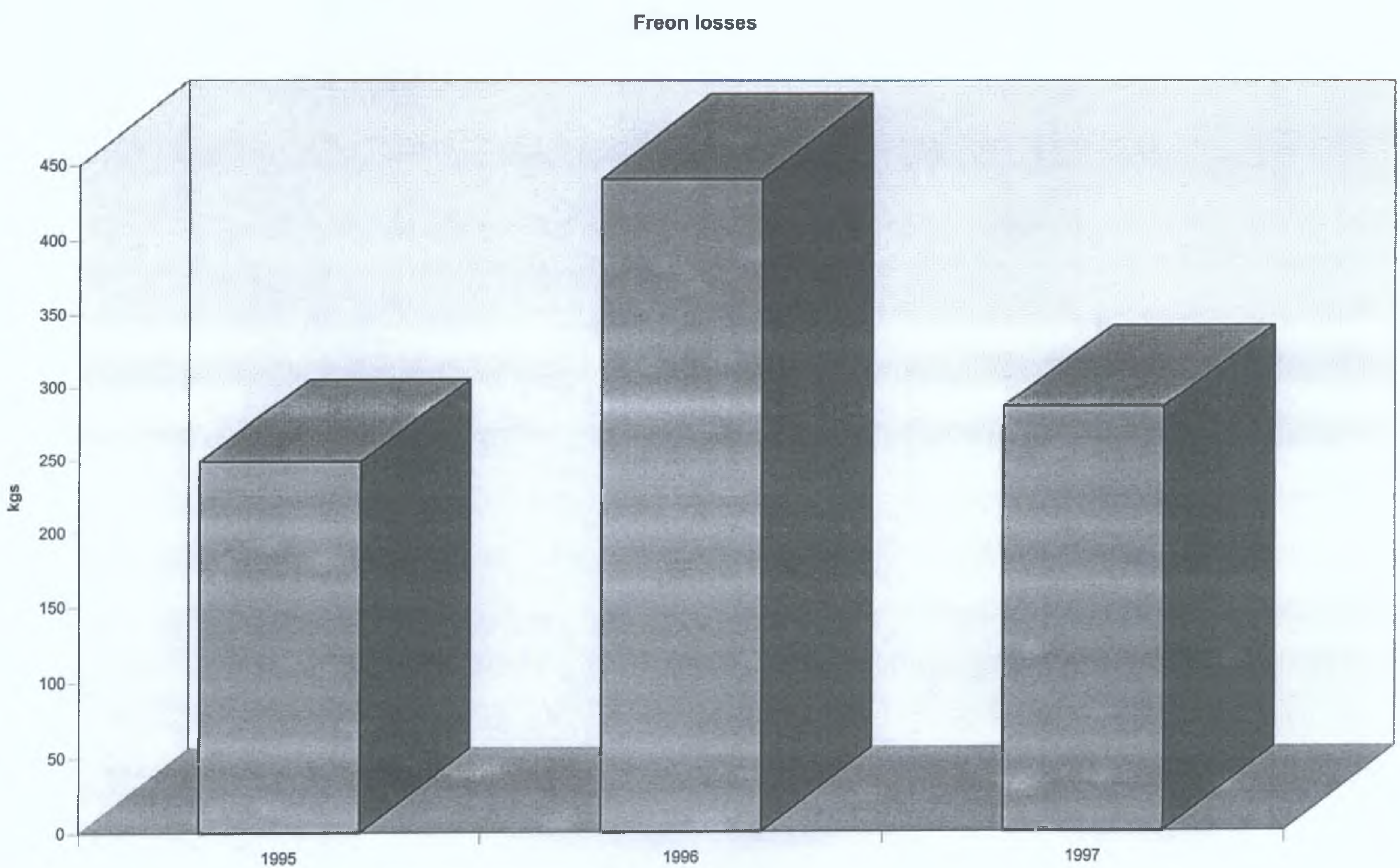

Freon losses
kgs
450
400
350
300
250
200
150
100
50
0
1995
1996
1997

Fig 6

5.0 WASTE MINIMISATION TECHNIQUES

We will now look at some of the techniques for waste minimisation in the Bulk Pharmaceutical Industry. Fig. 7 summarises possible waste minimisation techniques. The techniques can be broken down into four major categories as follows:

* Inventory Management
    -- inventory control
    -- material control

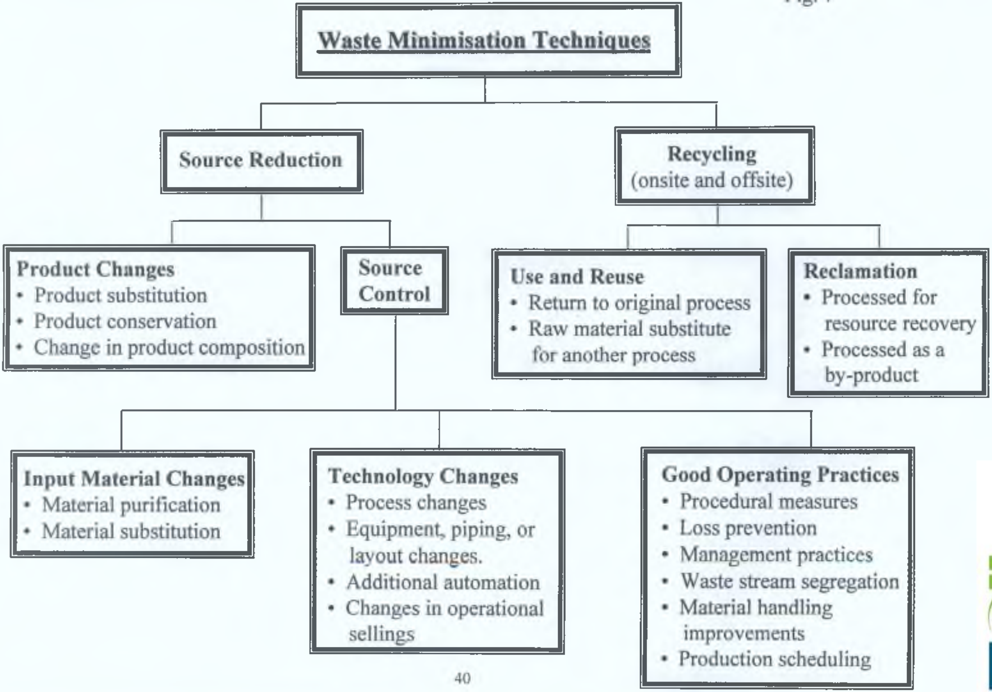
* Production Process Modification
    -- operational and maintenance procedures
    -- materials change
    -- process equipment modification

* Volume Reduction
    -- source reduction
    -- concentration

* Recovery
    -- on-site
    -- off site

The first three categories detailed above can be classified under source reduction and the last one under recovery/reuse in the waste minimisation. It should be noted that waste reduction techniques are generally used in combination so as to achieve maximum benefit at the lowest cost. It is important to realise that the impact of a waste reduction technique on all waste streams must be considered. For example switching from a solvent based system to a water based system may result in lower volatile organic carbon emissions to atmosphere but can lead to an increased load on the wastewater treatment plant.

Fig. 7


Waste Minimisation Techniques
Source Reduction
Recycling (onsite and offsite)
Product Changes
• Product substitution
• Product conservation
• Change in product composition
Source Control
Use and Reuse
• Return to original process
• Raw material substitute for another process
Reclamation
• Processed for resource recovery
• Processed as a by-product
Input Material Changes
• Material purification
• Material substitution
Technology Changes
• Process changes
• Equipment, piping, or layout changes.
• Additional automation
• Changes in operational sellings
Good Operating Practices
• Procedural measures
• Loss prevention
• Management practices
• Waste stream segregation
• Material handling improvements
• Production scheduling

5.1 Inventory Management

5.1.1 Inventory Control

Inventory Management involves techniques to reduce inventory size and hazardous chemical use while increasing inventory turnover. Proper inventory control can help reduce wastes occurring as a result of:

* excess materials
* out-of-date materials
* redundant materials
* residual in packaging materials
* type and size of containers
* type of packaging

Methods which can be employed to reduce waste include:

* A "just in time" inventory control system
* Computerised inventory control and materials issue system to give close liaison inventory control and production requirements .
* Specify packaging materials with a low "cling" factor.
* As far as possible have the active materials supplied in quantities to match the production batch size and thus avoid generating partially full containers. Change from small volume containers to bulk or reusable containers

5.1.2 Material Control

It is important to have proper control over the storage of raw materials, intermediates, products and process waste and also the transfer of these items within the process and around the facility. This will minimise losses through spills, leaks or contamination. It will also ensure that the material is efficiently handled and used in the production process and dose not become waste. The following specific techniques will help to minimise losses.

* Clear operating procedures for good housekeeping and material handling and proper training in same.
* Use of vapour balancing line during filling of bulk solvent tanks.

* Blow through fill lines.
* Fit conservation vents to solvent storage tanks.
* Fit overfill protection to solvent storage tanks.
* Regular maintenance programme to check lines, valves and pumps for leaks.
* Utilise pumped rather than pressure transfers between vessels.
* Control of storage conditions e.g. temperature, humidity
* Use of dedicated tanks and vessels to reduce decontamination.
* Segregation of waste streams to avoid cross - contamination of hazardous and non-hazardous materials and to increase recoverability.
* Regular calibration of weigh scales and flowmeters to ensure accurate dispensing.
* Collection of spilled or leaked materials for reuse.
* Avoid the use of open top containers for transporting material about the site.
* Enclosed solids charging systems
* Detection systems for solvent leaks.
* High integrity bund system for bulk solvent storage.
* High integrity (double contained) underground waste lines.

In the Bulk Pharmaceutical Industry a wide variety of solvents are used in the process. The greatest environmental threat arises from operations involving solvents. Tables 4 and 5 detail the various operations, the areas of potential losses and measures which may be adopted to minimise these losses.

5.2 Production Process Modification

Wastes can be significantly reduced by improved process efficiency. Such improvements can range from simple inexpensive changes in production procedures to the installation of state -of -the art equipment. Three techniques for production process modification have been identified. These are improved operation and maintenance, material change and equipment modification.

TABLE 4
OFF-LOADING / STORAGE

SOLVENTS	POSSIBLE ENVIRONMENTAL EFFECTS	MEASURES ADOPTED TO ELIMINATE / REDUCE EFFECT
OPERATION		
Tanker off-loading	Loss of liquid @ hose connection loss to atmosphere or drains	•Quickfit connections on all hose connectors with appropriate seals
Pumping from tanker to storage tank	Loss to atmosphere, drains from pump seal.	•Seal less pumps
Tank filling	Overflow with loss of liquid.	•Level gauge with indication, high level alarm and cut out on feed line.
	Loss from leak on level gauge	•Sealed gauge with magnetic follower.
	"Breathing" loss from vent due to displacement.	•Conservation vent to limit emission.
		•Tank vented to scrubber or carbon drum
Tank leak	Loss to atmosphere or to drains	•Bund wall to take any spillages (impervious) (licence requirements)
Tank overpressure	Catastrophic collapse of vessel	•Pressure relief safety valve
Tank vacuum	Possible collapse of vessel	•Vacuum breaker
Fire	Could be substantial	•N_2 purge for flammable solvents. Tanks have a deluge system to arrest the development of a fire.

TABLE 5
TRANSFER OF RAW MATERIAL FROM STORAGE TO PROCESS

OPERATION	POSSIBLE ENVIRONMENTAL EFFECT	MEASURES ADOPTED TO ELIMINATE / REDUCE EFFECT
Pumping from bulk tank to process vessels	Spillage from pump seal: •Atmospheric emissions •Ground water contamination	•Double mechanical seals •"Canned" pumps •Seal less pumps •Liquid low level pump cut out to avoid damaging the unit
	Spillages from flanges: •Atmospheric emissions •Ground water contamination	•Correct flanges gasketing for solvent being used. •Minimum number of flanges
	Overfill of vessel with solvent: •Possible contamination of drains	•Automatic cut out on meter after pre-set
SOLIDS Vessel charging	•Spillage of solids Process drain contamination	•Procedure drawn up for sweep up of solid & subsequent charging to reaction

5.2.1 Operation and Maintenance Procedures

Improvements in the operational area are usually relatively simple and cost effective and may lead to significant wastes reduction. the following areas are worthy of consideration:

* Reduce raw material and product loss due to spills, leaks and off-specification process intermediates.
* Schedule production to minimise vessel cleaning e.g. use dedicated equipment as far as possible.
* Improve cleaning procedures to reduce the generation of dilute mixed wastes with methods such as dry cleaning techniques, using mechanical wall wipers or squeegees and using nitrogen to clean lines.
* Segregate waste streams to increase recoverability.
* Optimise operational parameters (such as temperature, pressure,reaction time, concentration and chemicals) to reduce by-product or waste generation.
* Use a distributive control system(d.c.s.) to accurately control process parameters.
* Evaluate the need for each operational step and eliminate unnecessary steps.
* Control inertion by interlocking with oxygen meters.
* Use pumped rather than pressure transfers whenever possible
* Use closed charging systems.
* Develop employee training procedures on waste reduction. Develop motivational schemes for waste reduction.
* Collect spilled or leaked material for reuse.
* Develop clear and concise operating instructions.

A strict maintenance programme which stresses corrective and preventive maintenance can reduce waste generation caused by equipment failure. Such a programme can help spot potential sources of leaks and correct a problem before any material is lost. The programme may include cleaning, making minor adjustments, lubrication, calibration, recording energy usage and thermographic analysis of equipment. Scheduling of routine maintenance is greatly facilitated by the use of a computerised maintenance programme. (e.g. Idhammer system). With this system each item of equipment is given a tag number under which is recorded all of its history from the day it was purchased including its maintenance schedule, breakdown history, etc.

5.2.2 Material Change

Hazardous materials used in a production process e.g. raw materials, solvents, catalysts etc., may be replaced by less hazardous materials or even non-hazardous materials. Changes in input materials may also lead to a reduction in, or avoidance of, the formation of hazardous substances. The objective should also include a reduction in the quantity of waste generated. Examples include:

* The replacement of CFC'S with more ozone friendly products.
* The replacement of chlorinated solvents with non-chlorinated solvents e.g. acetic acid, ethyl acetate.
* The replacement of solvent based cleaning with water based cleaning.
* Substitution of chemical biocides in cooling water systems with alternatives such as ozone or u.v.
* Reduction of phosphorous in wastewater by reduction in the use of phosphorous containing chemicals.

As previously mentioned care must be taken to examine the impact of changes on the total waste from a process. This is particularly important in the case of material changes. The effect on aqueous wastes of changing from organic solvents to water is a case in point.

5.2.3 Process Equipment Modification

Waste generation can be reduced by thorough process modification or modernisation. Process modifications involves changes in process equipment and/or changes in operating parameters. Modernisation includes installing updated control mechanisms or increasing control levels. Increasing process automation (computerisation) is another form of modernisation. Examples include:

* Introduction of new process equipment which is inherently cleaner e.g. dry running vacuum pumps, magnetic drive pumps.
* Use back pressure valves on vessels and reactors to minimise vapour losses. Installation of vapour recovery systems to return emissions to the process.
* Optimisation of control parameters such as flow, temperature, pressure by the installation of a computerised (d.c.s.) control system. This will lead to increased reactor efficiency and reduce by-product formation. It will also help to reduce operator errors.
* Redesigning chemical transfer systems e.g. replacing nitrogen transfers with pumped transfers eliminates the vessel pressurisation step and its associated material losses.
* Redesign of equipment and piping to reduce the amount of material to be disposed of during start-ups, shut-downs, product changes and maintenance programmes.
* Better column design to reduce the quantity of top and bottom wastes.
* Modify reactor and vessel design to minimise clingage.
* Use liquid ring vacuum pumps with liquid recycling.
* Use of reactor/filter/dryers to minimise separations and handling and thereby reduce waste.
* Use of more efficient motors and speed control by the use of frequency inverters to reduce energy consumption.
* Use overfill protection devices on vessels.
* Use clean-in-place (cip) systems.

While significant waste reduction can be achieved there are barriers to process modifications. Extensive process changes can be very expensive, capital outlay may be required. Down time will occur when production is stopped for new equipment installation. New processes must be tested and validated to ensure that the resulting product is acceptable. If there are changes to the drug master file (D.M.F.) regulatory approval may be required which may be lengthy and expensive. In addition management may be reluctant to change a working process.

5.3 Volume Reduction

While reduction in volume dose not, in itself, constitute waste reduction, it frequently facilitates separation and recovery. The two techniques commonly employed are source segregation and concentration. Source segregation is a basic tenet of waste minimisation. The segregation of wastes allows them to be more readily removed or recovered. A common problem in the Bulk Pharmaceutical Industry is the recovery of pure solvent from a matrix of waste solvents. The problem is particularly difficult for solvents with similar boiling points and solvents which form azeotropic mixtures. It is much easier to recover a single solvent that is , for example, contaminated with product or even water. It makes sense therefore to segregate waste solvent streams as far as possible. Another example is the mixing of small quantities of organic solvents with aqueous streams. This has the effect of making it uneconomical to recover the organic stream and also puts an increased load on the plants biological waste water treatment facility. Sometimes it may be possible to segregate washwater or solvent used to clean process equipment (lines, vessels, reactors) for reuse in the process, but this practice is not very common in the Bulk Pharmaceutical Industry because of G.M.P. restrictions. Another example of source segregation is the utilisation of acid or alkali wastes from the process for pH adjustment in the waste water treatment plant.

The Concentration of wastes involves the removal of some portion of it to make more amenable for recovery or easier disposal. There are many techniques for carrying out this operation, for example, filtration, reverse osmosis, ultrafiltration, vaporisation, drying, compaction etc.,. Examples are the stripping of aqueous streams to remove chlorinated solvents to make the stream suitable for biological treatment, the recovery of catalysts by filtration, the drying of waste water treatment plant sludge to make it suitable for composting.

5.4 Recovery

Recovery of waste streams for recycle and reuse in many circumstances provide a cost effective alternative to treatment and disposal. It should be emphasised however that the elimination and minimisation of waste at source are the preferred options in the hierarchy of waste management practices. Nevertheless there will always be some waste generation -the concept of zero waste dose not exist in practice- and recovery represents a viable waste management alternative, especially in the context of sustainable development. Effective recovery is facilitated by the segregation of waste streams as discussed above.

Recycling and recovery includes direct reuse of the waste material , reclamation by recovering secondary materials for a separate use, and removing impurities from waste to obtain a relatively pure substance. The goal of this option is to recover materials for reuse in the process or for reuse in a different application. Because of G.M.P. requirements recovered solvents in the Bulk Pharmaceutical Industry require a high degree of purity. There are restrictions in the use of recovered solvents, for example, for the final step of a synthesis, crystallisation must be carried out from virgin solvent. The Bulk Pharmaceutical Industry produces large quantities of used solvents and this area presents the greatest opportunities for recovery. The Environmental Protection Agency place great emphasis on solvent recovery in I.P.C. licensed facilities.

Recovery may be on site or off-site depending on the nature and scale of the facility. On site recovery is preferable, since it reduces possible handling losses and allows the management of the waste to remain within the control of the plant.

5.4.1 On-site Recovery

On-site recovery can be an integral part of the process, for example stripping off of solvent to facilitate in crystallisation will result in a pure solvent which can be reused in the process. It is common practice in the Bulk Pharmaceutical Industry to have dedicated solvent recovery plant. The most popular technique for solvent recovery is distillation. Distillation processes may operate in batch, semi-batch or continuous mode. The type of operation selected depends on the quantity and the type of waste to be distilled. In the Bulk Pharmaceutical Industry batch distillation is the most common technique as it integrates well with the batch nature of this industry. In batch distillation the waste solvent is heated in a still pot, the solvent is boiled off, condensed and stored for reuse. Usually the bottom and top fractions are not reused. The still bottoms are removed for disposal. Solvent recovery can be single or multi-stage depending on the complexity of the separation required.Solvents commonly recovered are chloroform, dichloromethane, pyridine, toluene, methanol. methyl ethyl ketone, acetone, ethyl acetate, cyclohexane.

Other examples of recovery/recycle are:

* Wastes which have physical or chemical properties suitable for other on-site applications, for example the use of a caustic waste stream to neutralise an acid waste stream or vice versa.
* The use of waste solvents or waste oils as a boiler feedstock.
* Reuse of extracted water, for example from an reverse osmosis unit.
* Recovery of catalysts.
* Reuse of containers, for example the reuse of 200L drums for waste storage

5.4.2 Off-Site Recovery

Wastes may be considered for reuse or reclamation off-site when:

* Equipment is not available on-site to do the job.
* The scale of operations is such that on-site recycling would not be cost effective.
* The recovered material cannot be used in the production process.

In the Bulk Pharmaceutical Industry the greatest quantity of waste sent for off-site recovery/reuse are used solvents. In Ireland there are no facilities for the recovery of solvent so the wastes must be exported for recover/reuse. The plant will usually deal through an Irish Broker who will arrange to have to have the waste treated by a dedicated recycling facility. Most of these facilities are located in the United Kingdom. Many used solvents may be valuable depending on current prices and the degree of contamination. The waste solvents may be sold to recovery companies, they may be given free of charge or they may be a nominal charge. Usually the waste generator will pay the transportation costs. (which may be considerable). The recovered solvent may be subsequently sold for secondary applications. Many of the hydrocarbon solvents that are recovered are used as paint thinners or are mixed into large volumes of petrol, for example xylenes, toluene, heptane, hexane, cyclohexane etc. Many of the chlorinated solvents that are recovered are used in paint thinners or as degreasing agents, for example dichloromethane. Acetone is used in the fibreglass industry. Solvents with a high calorific value can be used as a fuel in cement kilns.

Other materials that are recovered off-site include:

* Waste lubricating oils.
* Metal drums for steel recovery.
* Mercury from luminescent lamps.
* Waste paper, glass, aluminium cans.
* Bioplant sludge for the manufacture of compost.

6.0 CASE STUDY

6.1 Company profile

Company A is located on a 28 acre site on the Little Island Industrial Estate in Co.Cork. It was established in 1974 and is a wholly subsidiary of a multi-national pharmaceutical company. It generates a turnover of 24 million pounds annually and employs 90 people. The company specialises in the manufacture of bulk pharmaceuticals and in particular, products for the treatment of cancer, c.n.s. products and smoking cessation aids. These products are manufactured by chemical synthesis for use in formulation plants for the preparation of ampoules, tablets and other such dosage forms. The company's products could be described as high in value and low in volume. The total output from the plant is approximately 30 tons/year. The plant essentially consists of administration offices, production facilities, (six production buildings), laboratories, utilities, warehouse, tank farm, maintenance workshop and waste water treatment plant. All products are manufactured by the synthesis of organic compounds using batch processes. Raw materials in the form of liquid solvents and reagents, organic and inorganic solid reagents and some gaseous compounds are reacted in a series of processing steps contained within the process buildings.

6.2 Principal Sources of Waste

The principal sources waste generated by the plant are:

* Mother liquors, solvents and unwanted by-products from the production process which remain when the desired product has been isolated.
* Waste liquids from unit operations.
* Solvent waste from the cleaning of process equipment.
* Waste oils from the vacuum pump circuits.

* Samples of hazardous materials taken by the Quality Control laboratory for testing.
* Solid hazardous waste from where inert material has been in contact with raw materials, intermediates or products. This includes both liquid and air filter media, raw material containers, packaging materials and protective clothing.
* Waste water treatment plant sludges.
* General trash.

6.3 Company Policy on Waste

At corporate level the company is committed to the minimisation of waste and the conservation of natural resources. This commitment is embodied in the corporate environment policy by the following statement:

Our challenge- our ambition - is to save lives and enhance living while protecting the environment from any harm that could result from the research, development, manufacturing, packaging, distribution, use and disposal of our products. We will preserve the earth's resources for the benefit of future generations.

We will aim for innovative and environmentally sound technologies, products and packaging.

We are committed to conserving natural resources and preventing pollution by reducing wastes at their source, reusing and recycling materials and disposing of waste safely.

We will expect our suppliers performance to be consistent with this policy.

At local level company A's environmental policy is consistent with the above policy.

Company A is a wholly owned subsidiary of Company A Incorporated and is involved in the manufacture Pharmaceutical Products which make an important contribution to the health care industry. It is the policy of Company A to carry out its operations in such a way so as to minimise its impact on the environment, to *be open and communicative with the community in which it operates and to involve all its employees in environmental awareness.*

We will achieve this by:
** Complying fully with all applicable environmental legislation and where possible exceeding regulatory requirements.*
** To monitor the impact of its activites on the environment and to ensure that it is minimised.*
** To foster openness and dialogue with employees and the public about our environmental performance. We shall respond to those concerns about the potential hazards and impacts of operations, products, emissions and waste.*
** Minimising as far as possible the generation of waste and the consumption of raw materials and energy.*
** Encouraging similar environmental standards to our own from all third parties involved with our business - suppliers, contractors and vendors.*
** Striving for continual improvement through the setting of measurable annual environmental targets, auditing performance and publishing results.*

6.4 Setting up the Program

To give concrete effect to the principles enunciated in the above policy statement (which was signed by the Managing Director) senior management gave full backing to the setting up of a waste minimisation programme. The first step was to form a waste minimisation team consisting of:

Environment and Risk Manager
Maintenance Manager
Logistics Manager
Production Manager

There was also set up a reference or steering group consisting of :

Managing Director
Quality Assurance Manager

Research and Development Manager
Finance Manager

The first task of the team was to communicate the ethos of waste minimisation throughout the company. This took the form of a slide presentation and covered the elements of a waste minimisation programme as detailed earlier in this report. The Environmental and Risk Manager was the senior management representative on the team and was the champion of the waste minimisation programme.

The next step for the team was to review all aspects of the company's operations and from that review establish a series of objectives and targets for waste minimisation. As a result of the review it was decided to investigate the following areas for waste minimisation.

* Solvent loss
* Use of hazardous materials
* Materials to landfill
* Energy conservation
* Water use
* Packaging materials
* Waste oils
* Use of CFCs

For each of the above areas a waste minimisation sub-team was established. Each team had at least one expert on the subject area being studied and they evaluated the waste minimisation potential for each of the above areas.

6.5 Solvents

The company utilises the following solvents in its processes:

Ethanol
Methanol
Isopropyl Alcohol
Chloroform
Dichloromethane

Pyridine
Methyl Ethyl Ketone
Toluene
Acetone

The bulk of the company's hazardous waste is composed of the above solvents. Progress was made in the following areas.

6.5.1 Solvent Recovery- On Site

The company employ's two 2000 Litre batch stills for solvent recovery. Pyridine is recovered at a rate of 92% and dichloromethane at rate of 84%.
Isopropyl alcohol is recovered at a rate of 50%. The only solvent which has a major usage and is not presently recovered is ethanol. This is currently under investigation but its recovery is complicated by the fact that it forms azeotropes with water and other solvents. Also it is the main solvent for final product isolation which restricts its use as a recovered solvent. Methanol is also being investigated for solvent recovery potential. Of the other solvents listed the volumes were considered to be too small to merit further investigation.

6.5.2 Solvent Recovery- Off Site

A solvent recovery company was identified in the U.K. which would take mixtures of solvents with the predominant fraction being dichloromethane. The recovered dichloromethane is used in secondary manufacturing processes, for example, in paint thinners. The company also identified a company in the U.K. who purchase waste solvents for blending for subsequent use as a fuel for cement kilns.The solvent waste must have a high calorofic value and a chlorine content of less than 3%. At the time of writing there is a temporary halt to this outlet as a result of concerns relating to the lack of controls and monitoring in comparison to commercial incinerators.

The substitution programme involved extensive laboratory trials and pilot batch runs. Dichloromethane was identified as a substitute and after an comprehensive validation programme to satisfy regulatory requirements it was successfully introduced in the process. The overall programme took over two years to complete and cost in the region of £400,000.

An external consultant was engaged to set up an Pollution Emissions Register. The solvents looked at were toluene, dichloromethane and methanol. These solvents were tracked through all stages of the production process using the Mass Balance technique. As a result of this study the company will be in a position to identify areas of losses and thereby target these areas for further investigation. Eventually this technique will be applied to all the hazardous materials on site.

6.7 Reduction of Materials sent to Landfill

This area was selected because of the escalating cost and future availability of landfill as a waste disposal option. This is especially the case for the cost of landfilling bioplant sludges in the Cork area where costs have escalated dramatically over the past four years. (see Fig. 8)

In this category the company instituted the recycling of waste paper and aluminium cans. While these materials are not significant in the context of the overall quantity of waste on the site, nevertheless, they are important in that they help in generating a 'waste minimisation culture' in the company. They give a visible indication of waste minimisation and help to achieve early success for the program. Both of these programmes are run in conjunction with Rehab. In future it is planned to investigate the recycling of glass and plastic.

A programme has been set up to investigate the possibility of converting the bioplant sludge into compost. Initial trials have been encouraging on the use of the compost for forestry. It is planned also to study the technique of advanced fluidized composting. This technique utilises thermophilic aerobic biological treatment to treat sludge and convert it ultimately into carbon dioxide and water with over 90% conversion claimed.

6.8 Waste Oil Recovery

All waste lubricating and vacuum pump oils are sent off site for recovery and reuse. The recycle company is located in Ireland.

6.9 Metal Drums

Metal drums are decontaminated and crushed and sent to the local steel mill for use as scrap metal. Some of the drums are reused several times within the site prior to crushing and disposal.

6.10 Energy

The main energy sources on site are natural gas and electricity. An energy conservation programme was set up and it included:

* Monitoring the main users on site
* Installing inverters on the waste water treatment surface aerators
* Installing ' building management systems ' in new buildings
* Switching off air handling systems when buildings are not in use

The consumption of gas and electricity for the years 95/96/97 is detailed in Fig. 9.

6.11 Water Consumption

The vacuum pumps were identified as major sources of water consumption. The older vacuum pumps on the site are of the water ring type and require a constant flow of to operate. A programme has been set up to install a recirculation system on these pumps which will result in a reduction of water consumption of the order of 50%. Also all new vacuum pumps will be specified as dry running or oil ring.

A programme was instituted to:

* Switch off water consuming plant when not in use
* Repair leaks from valves, pumps, hoses etc.
* Switch off hoses when not required
* Fit trigger valves to all hoses

Fig 8 Sludge Disposal costs

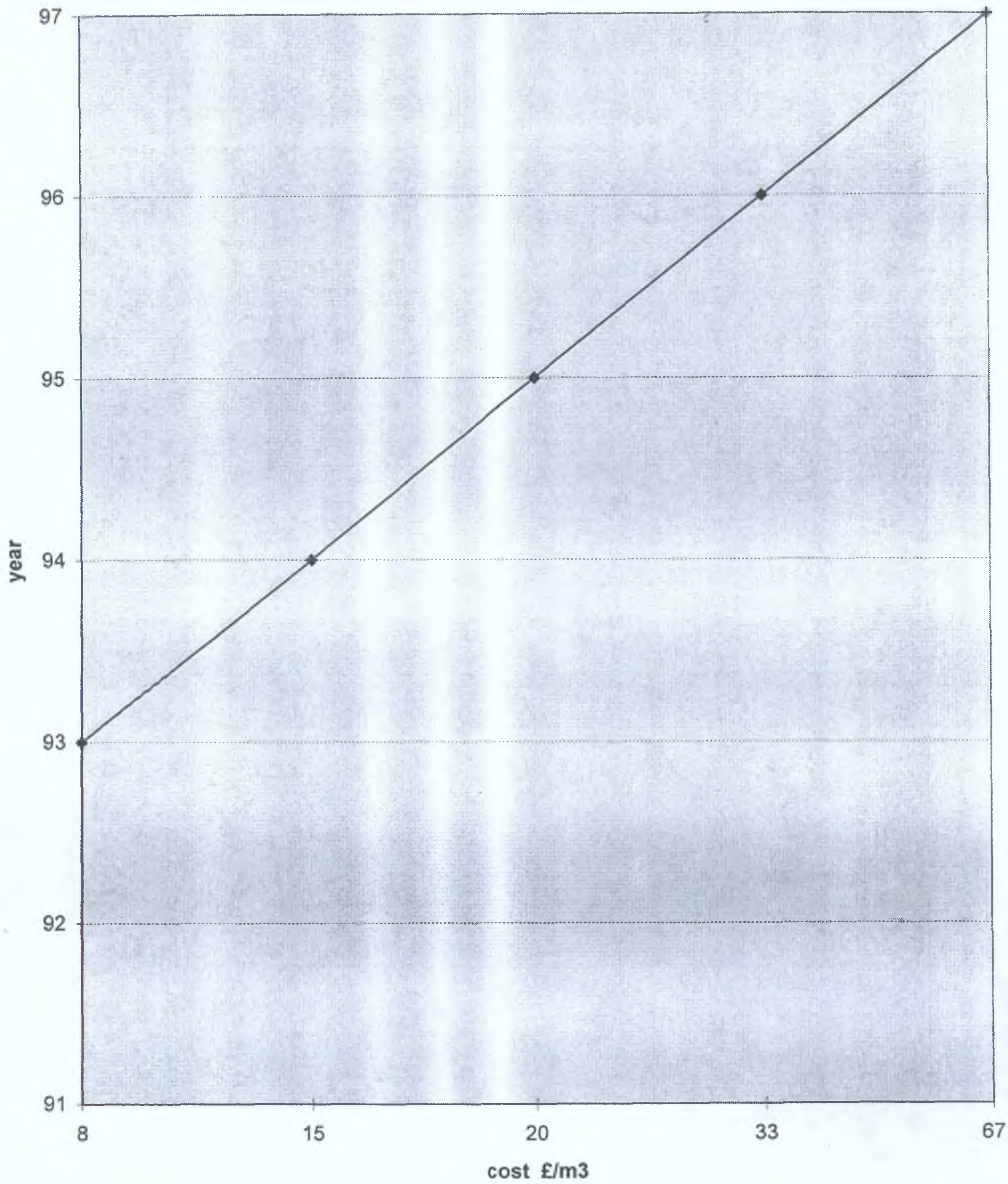
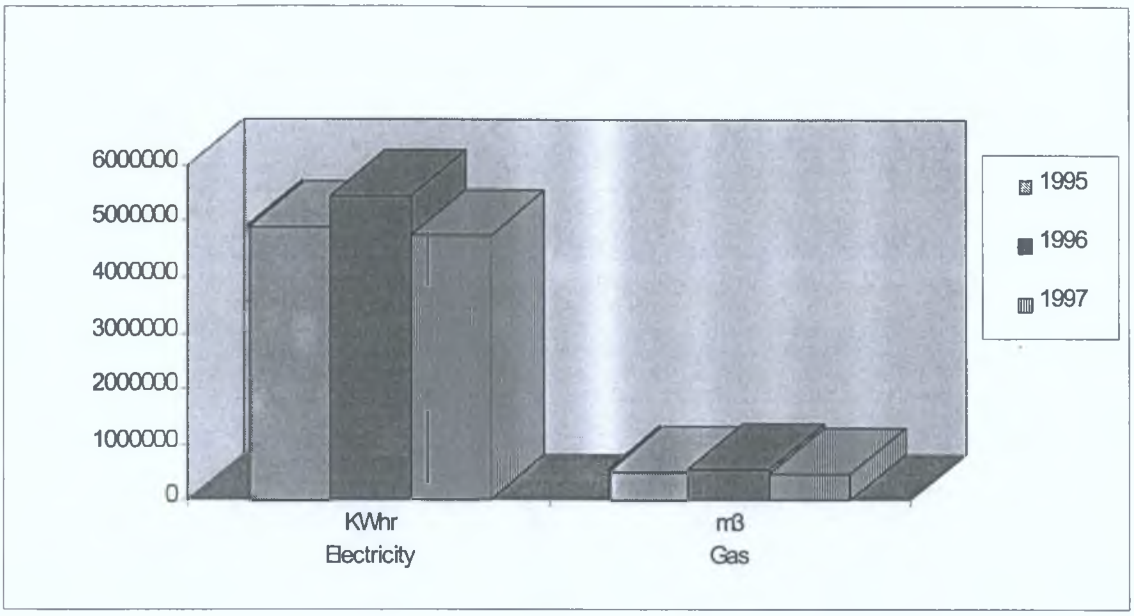


Fig. 9 Electricity and gas usage



7.0 CONCLUSIONS

7.1 The disposal of waste has become a serious strategic issue for the Bulk Pharmaceutical Industry in Ireland. The problem has been brought clearly into focus by the lack of any facility in Ireland for the disposal of hazardous waste and also by the increased cost and lack of outlets for the disposal of non-hazardous waste.

7.2 Because of the above, companies are moving from the traditional end-of-pipe technologies to a clean technology and waste minimisation approach.

7.3 For any waste minimisation programme to succeed it must have the commitment of top management and must be understood and supported throughout the company.

7.4 Best results can be achieved if a systems approach is adopted for implementing a waste minimisation programme.

7.5 A large proportion of the hazardous waste generated by the Bulk Pharmaceutical Industry is used solvents. A large fraction of this solvent is recovered for re-use. The main recovery technique is distillation.

7.6 Because of regulatory constraints there are restrictions on the re-use of solvents. Also process changes may require extensive re-validation even for minor changes.

7.7 In common with other industries the Bulk Pharmaceutical Industry is actively involved in recycling paper, plastics, and other materials.

References

1. Facility Pollution Prevention Guide, United States Environmental Protection Agency, Office of Research and Development, Washington, DC 20460.
   May 1992

2. Waste Audit Study, Drug Manufacturing and Process Industry, Prepared for Alternative Technology Section, Toxic Substances Control Division, California Department of Health Services.
   May 1989

3. Crittenden B.D., Kolaczkowski S.T., Waste Minimisation Guide For The Institution of Chemical Engineers With The Support of the Department of the Environment, Selectamaster Ltd., Bath, Avon.
   February 1992

4. Kiely Gerard, Environmental Engineering, McGraw-Hill.
   ISBN: 0-07-709127-2 *(1997)*

5. Rozich Alan F, Colvin P.E., Strom Dennis, Advanced Fluidizing Composting Offers an Alternative For Treating High Strength Wastes.

6. Cunningham Dermot, Moriarty Jim, Cleaner Technologies For The Fine Chemicals / Pharmaceutical Industry, Clean Technology Centre, RTC Bishopstown, Cork, Ireland.

7. Recent Developments in The Area of Environmental Protection, Environment Bulletin, Department of the Environment.
   November 1993

8. Butler Anne, Carty Gerry, Environmental Protection Agency Waste-A Major Challenge PP 22-24, Environmental Management Ireland.
   Vol. 1, No. 4, 1994.

9. Environmental Protection Bulletin, Institute of Chemical Engineers.
   Issue 049, July 1997

10. The Green Pages, The Newsletter of the Environment Service of IBEC.
    Vol. 1, No. 6, October 1997

11. Waste Disposal, Enfo, Fact Sheet 1.

12. Industrial Waste Management, A CEFIC Approach To The Issue, Conseil European des Federations de L'Industrie Chimique.

13. Huisingh Donald, 'Enhancing Economic Performance' First Cleaner Production National Conference 24-25 March 1993.
Cleaner Production Promotion Unit, Department of Civil & Environmental Engineering, University College, Cork.

14. Penninger Johannes Mr, Super Critical Fluid Technology, Potential in the Fine Chemicals and Pharmaceutical Industry.
Paper given at the workshop on Prevention of waste and Emissions in the Fine Chemicals/Pharmaceutical Industry, Cork, Ireland
October 4th, 5th, 1993

15. Sheldon, R.A., "Consider The Environmental Quotient", Chemtech, 38-47.
March 1994

16. CEFIC Guidelines on Waste Minimisation, 1990 Conseil European des Federations de L'Industrie Chimique, Avenue Louise 250/71 B-1050 Bruxelles.

17. Waste Management in Ireland, EPA Newsletter.
Vol. 4, No. 3, December 1997

18. National Waste Database - Report For 1995, Environmental Protection Agency, Wexford.

19. Striking The Balance, an Environmental Policy For Economic Growth, IBEC, Dublin.

20. Nolan W, Economic Impact Survey For The Irish Pharmaceutical and Chemical Manufacturers Federation, A Report By The Irish Business And Employers Confereration.
March 1995

21. Developments in the Area of Environmental Protection, Environment Bulletin.
Issue 37, February 1998, DOE

22. Cahir Maria, Byrne O'Clerigh Ltd., Cleaner Production Pilot Programme Environmental Management Ireland 2-5.
Vol. 4, No. 3, 1998

23. Cairncross Frances, Waste and the Environment, A Lasting Reminder, The Economist.
May29th 1993

24. Duff Nuer, Cleaner Production Implementation Techniques, IBEC Seminar: Increased Profits From Cleaner Production.
Dublin, 28 November 1996

25. Integrated Pollution Control Licensing Guidance Note For : Annual Environmental Report, EPA Wexford.
1997

26. Redman John, Pollution is Waste, The Chemical Engineer.
June 1989

27. Hutchinson John, Dowe David, Cleaner Manufacturing Technologies in Ireland. Prepared For The Department of Environment.
October 1993