Resource Efficiency in Priority Irish Business Sectors

RESOURCE EFFICIENCY FACTSHEET

Pharmaceutical & Chemical Sector

The sector

The sector is very significant from a financial perspective in Ireland; the net sales value (NSV) of basic pharmaceutical products and preparations in 2016 was €58.3 billion[1] (the total value of products manufactured and sold in Ireland in 2016 was €133.3 billion). The pharmaceutical and chemical sectors accounted for 55.8% of NSV from Irish manufacturing in 2016, with the pharmaceutical sector, NACE 21, on its own contributing 43.7% of total NSV (the total value of products manufactured and sold in Ireland in 2016 was €133.3 billion – or 48% of Ireland's GDP).

Eight of the top ten pharmaceutical manufacturers in the world have plants in Ireland[2]. These plants range from primary production of bulk pharmaceutical production facilities (active pharmaceutical ingredients (API) or biopharmaceuticals/ biologics) to secondary production with companies that produce finished pharmaceutical products.

Policy

At the time of writing the EU Commission is seeking input from stakeholders on the EU Circular Economy Action Plan[3]. CEFIC, the European Chemical Industry Council, has recommended to the EU that it:

- Apply the "safety first" principle to the circular economy.
- Clarify the concept of waste and that of by-products under the Waste Framework Directive. The latter should not hinder further use of valuable materials.
- Remove the barriers (e.g. custom duties and technical barriers) preventing European companies from having fair access to renewables on the international market.

Under the EU REACH Regulation there is already guidance[4] in place on waste and recovered substances. Prevention of Environmental Impact is incorporated into EPA Guidance for IPPC licensees[5] in the pharmaceutical and chemical sectors. It includes consideration of:

Green Chemistry: Process design focusing on alternative synthetic routes and reaction conditions to utilise more environmentally friendly processes.

Solvent Selection: Careful consideration and selection of solvents during process development to prevent and minimise environmental impact associated with solvent usage.

Extraction from Natural Products: Minimise environmental impact of extraction process by using alternative extraction techniques, maximising extraction yield, and/or selection of optimum extraction solvent.

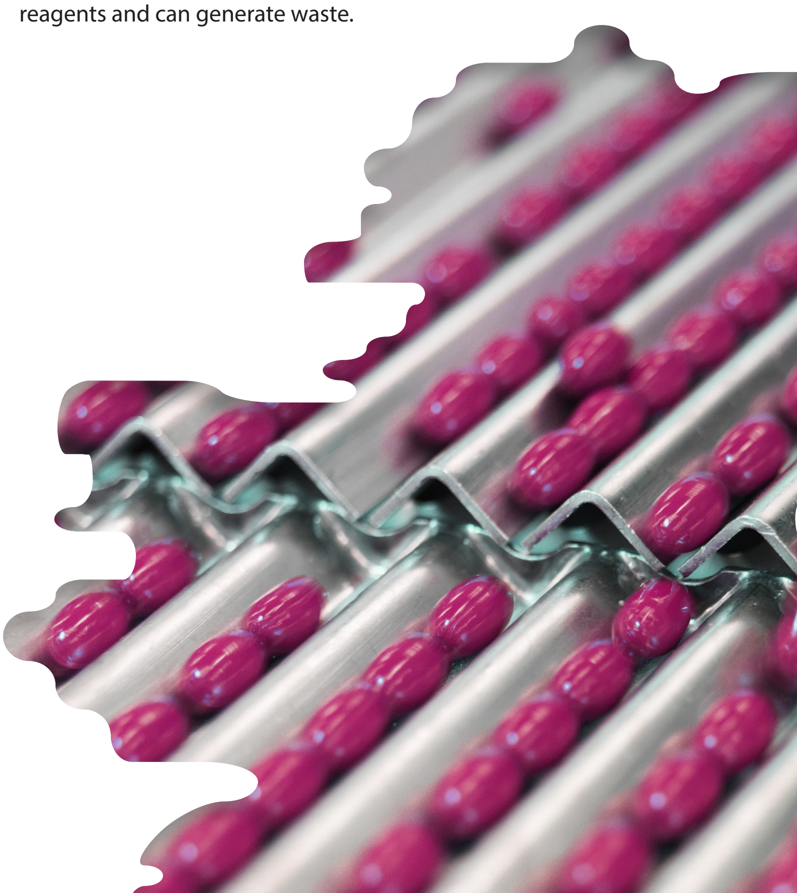
[1]http://www.cso.ie/en/releasesandpublications/er/iips/irishindustrialproductionbysector2016/
[2]https://www.enterprise-ireland.com/en/Source-a-Product-or-Service-from-Ireland/Sector-and-Company-Directories/Pharmaceutical-Sector-Profile.pdf
[3]http://ec.europa.eu/environment/circular-economy/index_en.htm
[4]https://echa.europa.eu/documents/10162/23036412/waste_recovered_en.pdf/657a2803-710c-472b-8922-f5c94642f836
[5]http://www.epa.ie/pubs/advice/bat/BAT%20Guidance%20Note%20Pesticides%20Pharmaceuticals%20&%20Speciality%20Organic%20Chemicals.pdf

Potential resource efficiency initiatives

The manufacture of pharmaceuticals and chemicals is associated with the generation of large volumes of waste including large quantities of hazardous wastes. There is significant energy expended in the storage, transport, treatment and transformation of these wastes. To improve resource efficiency in the chemical and pharmaceutical sectors the twelve principles of Green Chemistry were developed by Anastas and Warner in the mid-1990s. The principles followed on from work Anastas and his colleagues at the USEPA had been doing on the concept of benign by design.

The use of Green Chemistry principles, waste minimisation and cleaner production are approaches that can result in significant reductions in resource consumption in the sector. Some of these approaches include:

- Developing processes requiring fewer steps.
- Synthetic methods designed to maximise the incorporation of all materials used in the process into the final product (atom economy).
- The use of feedstocks having fewer inherent by-products and/or renewable feedstocks.
- More efficient equipment design, including better mixing.
- The ability to operate at lower temperatures and/or pressures
- Unnecessary derivatisation (use of blocking groups, protection/ de-protection, temporary modification of physical/chemical processes) should be minimised or avoided if possible, because such steps require additional reagents and can generate waste.



12 Principles of Green Chemistry

1. Prevent waste
2. Atom economy
3. Less hazardous synthesis
4. Design benign chemicals
5. Benign solvents and auxiliaries
6. Design for energy efficiency
7. Use of renewable feedstocks
8. Reduce derivatives
9. Catalysis (vs. stoichiometric)
10. Design for degradation
11. Real-time analysis for pollution prevention
12. Inherently benign chemistry for accident prevention

Molecular level tools used to measure the effectiveness of implementation of the 12 Principles of Green Chemistry include effective mass yield, measures of atom economy or efficiency, reaction mass efficiency and carbon efficiency.[6]

GREEN CHEMISTRY CASE STUDY: METATHESIS

Three researchers were awarded the 2005 Nobel Prize in Chemistry[7]: Dr. Yves Chauvin, Professor and Professor Richard R. Schrock, for the development of the metathesis method in organic synthesis in which carbon-carbon double bonds are broken and formed catalytically. Metathesis is used daily in the chemical industry, mainly in the development of pharmaceuticals and of advanced plastic materials[8]. Using metathesis, synthesis methods have been developed that are:

- more efficient (fewer reaction steps, fewer resources required, less wastage),
- simpler to use (stable in air, at normal temperatures and pressures) and
- environmentally friendlier (non-injurious solvents, less hazardous waste products).

Metathesis represents a significant step forward for green chemistry, reducing potentially hazardous waste through smarter production.

Cleaner production mirrors many of the principles of green chemistry. It includes the use of cleaner technologies in the industry such as:

- Closed/continuous reactors
- Extractive reactions
- Catalysis
- Supercritical fluid extraction
- Membrane separation
- Ultra-efficient condensation
- Improved mixing and vortex technology (power fluidics)

CASE STUDY: TAKE BACK CHEMICALS

TaBaChem[9] is a service based business model where a chemicals supplier is paid for the function of a substance rather than the quantity. This aligns the economic interests of supplier and user, reducing the amount of substance used while optimising the effect. This cooperation and related price setting differentiates Take Back Chemicals from simple forward integration or outsourcing and encourages development and operation of new production processes.

Cleaner Production is defined by United Nations Environment Programme (UNEP) as the continuous application of an integrated preventive environmental strategy to processes, products, and services to increase overall efficiency, and reduce risks to humans and the environment. Cleaner Production can be applied to the processes used in any industry, to products themselves and to various services provided in society.

For production processes, Cleaner Production results from one or a combination of conserving raw materials, water and energy; eliminating toxic and dangerous raw materials; and reducing the quantity and toxicity of all emissions and wastes at source during the production process.

Other improvement/efficiency tools including Lean Manufacturing and Six Sigma are popular in the sector.

Relevant Indicators

Resource efficiency in the manufacture of pharmaceutical products is dependant on parameters such as the quantity of the batch being produced, size of the batch input, energy input, quantity of solvent and water used at each stage of a process. Relevant KPIs (Key Performance Indicators) used at the process level include:

- kWh of energy per kg of product produced
- kg waste per kg of product
- litres of water used per kg of product produced
- litres of solvent used per kg of product produced
- ratio of virgin solvent to recovered solvent

The **E factor** represents the amount of waste produced in the process, including solvent losses, process aids, and fuel (water is excluded from the E factor calculation). Estimates of the scale of production output and associated E factors of the chemicals and pharmaceutical sectors worldwide are given in the table below. As can be seen, the E factors for fine chemicals and pharmaceuticals is far higher than that for bulk chemicals.

[6] http://greenchem.uoregon.edu/ACSGoingGreenSite/PDFs/20050316WedAM/1364Hamel.pdf
[7] https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2005/advanced-chemistryprize2005.pdf
[8] https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2005/press.html
[9] https://www.royalhaskoningdhv.com/nederland/diensten/diensten-van-a-tot-z/take-back-chemicals/1215

Table 1: E factors in the chemical industry worldwide[10]

Industry Segment	Volume product (tonnes per year)	E factor (kg waste/kg product)
Bulk chemicals	10^4-10^6	<1-5
Fine chemicals industry	10^2-10^4	5->50
Pharmaceuticals industry	10-10^3	25->100

Materials
Approaches to consider here include substitution of materials with less harmful ones (e.g. replacing chlorinated solvents with water, supercritical fluids (e.g. liquid carbon dioxide) or non-chlorinated solvents.

Solvent substitution
The substitution of organic solvents with aqueous solvents where possible in the process will reduce the consumption of solvents being purchased in industry. The use of aqueous solvents is a positive from a human health perspective. Moreover, increasing efficiency and reducing waste can be achieved by reducing the actual quantity of solvent being used where possible and by constant regeneration/recovery of spent solvent.

Waste
Solid and liquid waste generated by this sector includes: solvent waste; waste containing pharmaceutical products and by-products; sludge from wastewater treatment; packaging waste; and general municipal type waste. Annual environmental reports (AERs) for Irish IPPC licensed companies were reviewed. Of a total of 362,965 tonnes of waste disposed of by IPPC (Class 5.16) licensed pharmaceutical manufacturers in 2014, 130,967 tonnes of this total is hazardous (i.e. 36%).

One of the main tenets of waste minimisation is source segregation; mixing wastes makes them more difficult to recover. After a Clean Technology Centre analysis of Annual Environmental Reports (AERs) for Irish IPPC licensed pharmaceutical manufacturers (Class 5.16) from 2014, it was noted that, from a total of 362,965 tonnes of waste disposed of, 130,967 tonnes (i.e. 36%) of this total was hazardous.
The following observations were made:
- Waste organic solvent in Ireland originates primarily from the pharmachem sector:
- About 96% of the solvent waste arisings occur in this sector;
- 90% of the solvent waste arising is accounted for by less than 20 companies;
- between 50% and 60% of the solvent waste occurs in six companies.

[10]Green Chemistry in the Pharmaceutical Industry, P. Dunn et al. Wiley VCH, 2010

Water
Water consumption in the sector is mainly used for cleaning, heat transfer and process (water for injection (WFI), solution makeup, fermentation, etc.) operations. Approximately 70% of water used is mains water, 12% is groundwater and 28% is abstracted surface water (source: IPPCL AERs).

Equipment Cleaning
The reduction of the cleaning frequency, the use of a final rinse as the pre rinse for the subsequent cleaning cycle and sufficient sterilising medium are ways of using water and resources effectively.

The use of spray heads with low volume and high efficiency should also be incorporated into equipment for more efficient cleaning.

Energy
Energy consumption in the sector is associated with service utilities (steam, hot water, water and wastewater treatment, heating, ventilation, and air conditioning), lighting and electrically driven process equipment.

Green Chemistry principles include Design for Energy Efficiency. They specify that the energy requirements of chemical processes should be minimised and, if possible, chemical synthesis should be conducted at ambient temperature and pressure.

CASE STUDY: CORK LOWER HARBOUR ENERGY GROUP (CLHEG) HARBOUR WIND TURBINES
The project involved the installation of three 3MW wind turbines, one in each site in SKB, Janssen Biologics and DePuy Synthes in Ringaskiddy, Co. Cork. Novartis are the fourth pharmaceutical manufacturer involved in the project but the construction of the wind turbine at that facility has been deferred.

Further Information

The twelve principles of Green Chemistry
https://www.acs.org/content/acs/en/greenchemistry/what-is-green-chemistry/principles/12-principles-of-green-chemistry.html

BAT (Best Available Techniques) Reference Document (BREF) "Best Available Techniques for the Manufacture of Organic Fine Chemicals"
http://eippcb.jrc.ec.europa.eu/reference/BREF/ofc_bref_0806.pdf

EPA BAT Guidance Note Pesticides, Pharmaceuticals & Speciality Organic Chemicals Sector
http://www.epa.ie/pubs/advice/bat/

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This factsheet is one of seven that accompanies the main report of the EPA research project: Efficiency in Priority Irish Business Sectors (2014-RE-DS-1). Other factsheets are available on the following sectors: Food and Beverage, Retail, Manufacture of Non-Metallic Mineral Products, Accommodation and Food Service. There is also an overall factsheet. The main report is available at www.epa.ie.

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