

# Closing-the-loop in pharma: How green chemistry, continuous manufacturing, and mono-materials are shaping tomorrow



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## Abstract

The pharmaceutical industry heals millions, yet before single tablet reaches patient, its production and packaging operations silently consume vast reserves of energy, water, and raw materials, leaving behind carbon and plastic footprints that demand urgent, systemic reform. This article summarizes journey towards sustainable pharmaceutical technologies, from green chemistry in synthesis of APIs to lifecycle assessment (LCA)-guided manufacturing & packaging design to circular end-of-life management. It covers continuous-manufacturing, process analytical technology (PAT) & green solvents as waste-reducing manufacturing methods, mono-material, biodegradable & smart packaging innovations that are changing primary & secondary packaging. 3R framework, extended producer responsibility (EPR), & zero liquid discharge (ZLD) are discussed, focusing on regulatory developments in India. New digital technologies, like Artificial intelligence (AI) & digital twins, are identified as enablers to achieve greener operations. The article concludes that sustainability isn't an option but a scientific & professional necessity when designing products & systems from outset to their end-of-life.

**Keywords:** Green Chemistry; Sustainable Manufacturing; Pharmaceutical Packaging; Lifecycle Assessment; Circular Economy; Pharmaceutical Waste Management

## 1. Introduction

The processes used to make & package medicines are resource-intensive, & modern health care relies on uninterrupted access to safe, effective medicines. Carbon footprint of healthcare systems is estimated around 3-8% of total, while medicine alone can make up between 20-25% of healthcare carbon footprint, depending on prescribing patterns & packaging choices (1). In this footprint, energy, water & organic solvents are significant inputs to pharmaceutical manufacturing, & packaging, which is used to ensure product safety & integrity, has traditionally been made from multilayer plastics & laminates that are difficult to recycle.

Change is being driven by regulation. EU's Packaging & Packaging Waste Regulation, among others, stipulates all packaging for medicinal products must be fully recyclable within 10 years, & several multinational manufacturers have made commitments to recyclable packaging that are also time-bound (2,3). Sustainability is no longer a downstream “green” add-on for pharmaceutical profession but must be designed in from the molecule up, with environmental performance being considered alongside efficacy, safety & cost at every development milestone. This article follows that journey, from API synthesis & manufacturing to packaging & finally to disposal, focusing on technologies & the regulatory environment that influences practice in India.

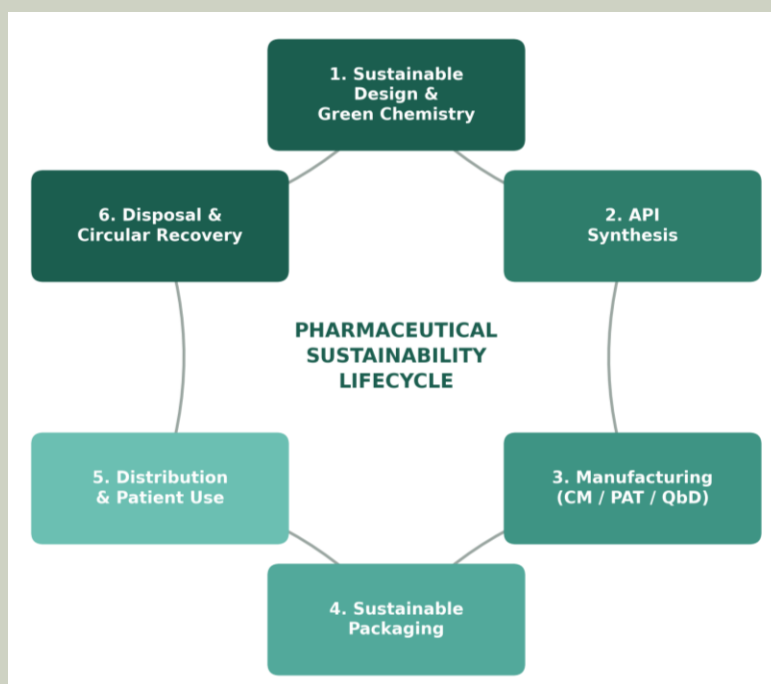


**Figure 1:** Pharmaceutical sustainability lifecycle

## 2. Green Chemistry & Sustainable API Synthesis

Multistep synthesis routes are frequently the most resource & waste-consuming step in manufacture of drugs, as significant number of hazardous by-products are formed (4). 12 principles of green chemistry are all about modifying synthetic routes, such as **Boots' 1960s** ibuprofen synthesis used stoichiometric aluminum chloride and zinc, producing 6 pounds of toxic waste per pound of drug; while **BASF's 1990s** catalytic route used recyclable palladium and solid acid catalysts, eliminating millions of pounds of waste annually. Common strategies include the use of renewable biomass feedstocks to decrease dependency on fossil carbon, replacement of toxic solvents with less hazardous solvents such as water & supercritical CO<sub>2</sub>, & biocatalysis(5). Compared to batch synthesis, continuous flow chemistry enables more precise control of temperature, pressure & residence time, which leads to higher yields, selectivity, lower solvent & energy use & is already used at scale in APIs such as celecoxib, valsartan & mesalamine (6). These routes are increasingly gaining acceptance by regulatory agencies such as US FDA & EMA for

their contribution to process robustness & product consistency, & this is slowly paving the way for their commercialization, in addition to their environmental advantages (6).

### **3. Lifecycle Assessment: The Quantitative Backbone**

To bring evidence and data into these design decisions, rather than relying on guesswork, industries are increasingly turning to Lifecycle Assessment (LCA), which is standardized under ISO 14040/14044 & quantifies environmental impacts over 4 stages: goal & scope definition, inventory analysis, impact assessment & interpretation, and raw material extraction to manufacture, distribution, use & disposal. The mean packaging-inclusive carbon footprint of over 12,000 oral medicines was 8.47 kg of CO<sub>2</sub> equivalent/medicine box, with significant variations in impact per medicine, depending on formulation & packaging type (1). Pharmaceutical packaging LCA studies usually consider over a dozen categories such as global warming, eutrophication, water & land use, etc.(7)

### **4. Sustainable Manufacturing Technologies**

#### **4.1 Continuous Manufacturing & Process Analytical Technology**

Continuous manufacturing (CM) replaces stop-start batch production with an uninterrupted material flow under a Quality-by-Design (QbD) framework, building product understanding throughout the process rather than only at the end. Compared to batch processes, CM delivers fewer synthetic steps, lower solvent and reagent use, reduced power consumption, and faster scale-up. **Eli Lilly**, an early adopter, demonstrated CM's sustainability case in practice: its continuous tablet manufacturing lines enabled measurable reductions in material waste and facility footprint while meeting FDA quality standards. Process Analytical Technology (PAT), using in-line near-infrared and Raman spectroscopy, complements CM by enabling real-time quality monitoring, immediate process corrections, and elimination of waste from batch rejections.(8)

#### **4.2 Green Solvents & Energy Management**

Solvent selection significantly influences manufacturing's environmental burden, driving a shift from toxic options like dichloromethane toward water, ethanol, and ionic liquids. Downstream purification and cooling water systems are being redesigned across the industry to cut both solvent and freshwater use per unit of product. A landmark example comes from **GSK**, whose second-generation manufacturing route for the cancer drug mCMAF reduced solvent consumption by 16,160 kg per kilogram of product, cut greenhouse gas emissions by 71%, and slashed energy consumption by 76%. (9)

### **5. Sustainable Packaging Innovations**

#### **5.1 Mono-Material & Recyclable Design**

Traditional blister packs are laminates of PVC, aluminum foil, & other polymers that provide good protection for the drug but are difficult to mechanically recycle. Industry's answer is mono-material packaging, in which packaging is constructed from a single polymer family, e.g. polypropylene, polyethylene terephthalate, or high-density polyethylene, which maintains barrier properties &

enables it to be recycled in conventional polymer streams. (fig. 2) This transition is supported by regulation: the EU's Packaging & Packaging Waste Regulation 2025/40 will mandate medicinal primary packaging be fully recyclable by 2034; manufacturers such as **Novartis & Merck KGaA** have established their own time-bound targets for packaging to be recyclable. (2,3)

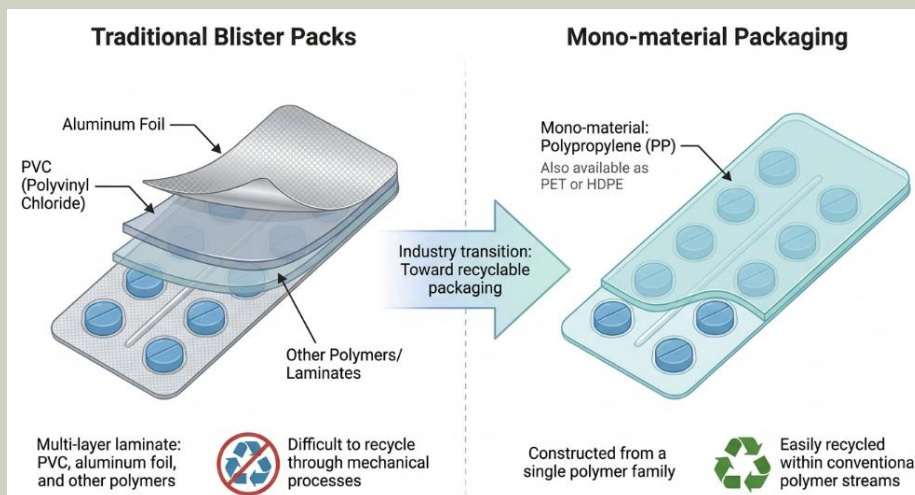


**Figure 1:** Shift from traditional to monomaterial packaging

## 5.2 Bio-Based, Biodegradable, & Smart Packaging

Research into bio-based polymers such as polylactic acid and polyhydroxyalkanoates for secondary and tertiary pharmaceutical packaging is advancing, alongside exploration of cornstarch-, sugarcane-, and cellulose-derived films where barrier requirements are less stringent. A milestone case study arrived in late 2024, when UPM Biochemicals, Selenis, and Bormioli Pharma jointly launched the world's first pharmaceutical bottle made from partially wood-based PET, using UPM's carbon-negative BioMEG and receiving European Pharmacopeia approval for global availability from Q1 2025. (10) Alongside materials innovation, smart packaging incorporating QR codes, RFID tags, and temperature indicators is strengthening anti-counterfeiting, supply-chain transparency, and patient safety, while also offering digital alternatives to printed package inserts.

## 6. Circular Economy & End-of-Life Waste Management

Closing the loop means something after the medicine leaves the pharmacy. Circular economy approaches in pharma are based on 3R principle (Reduce, Reuse, Recycle) Fig. 3

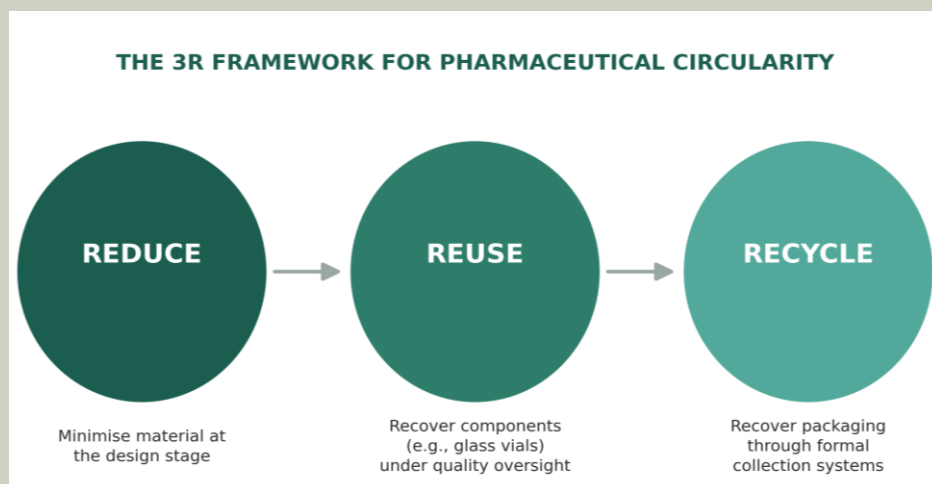


**Figure 2:** The 3R framework for sustainable pharmaceutical waste management.

Unused & expired medicines pose a significant but often overlooked environmental & public health issue. Improper disposal methods, such as flushing or throwing them in the trash, contribute to water & soil contamination & are linked to the global rise of antimicrobial resistance (AMR), a major public health threat (11). International agencies advocate enhanced national systems for safe medicine disposal, promoting pharmacy or drug take-back programs for appropriate incineration as a preferred solution. Advanced oxidation processes, activated-carbon adsorption, & zero liquid discharge systems are mandated in some areas for highly polluting industries like pharmaceuticals (12).

## 7. Emerging Technologies & Outlook

Artificial Intelligence and digital twins are transforming sustainable pharmaceutical manufacturing by predicting process deviations, optimizing energy use, and enabling real-time quality decisions without resource-intensive physical experimentation. AstraZeneca, operating across 26 global manufacturing sites, is a frontrunner: in 2026 it detailed how AI-agent-driven digital twins now arrange the full development pipeline from API to coated tablet, directly reducing waste by eliminating redundant physical trials. Roche is similarly deploying NVIDIA Omniverse-based digital twins to simulate and optimize biomanufacturing facilities before they go live, applying a "simulation first, construction second" principle. Looking ahead, on-demand 3D-printed dosage forms and AI-guided selection of greener synthetic routes in early R&D are set to extend these gains further.(13,14)

## 8. Challenges to Implementation

Despite this, adoption is still not widespread. The high capital costs of retrofitting & filing challenges uptake of sealing equipment & regulatory uncertainty about new materials. Even though the mono-material substrates have proven to be oxygen & moisture resistant, in moisture-sensitive applications, they offer a 27% shorter shelf life even when used in properties. Compared to multi-layer laminates, applications are used in greater numbers. Insufficient recycling facilities, local variations in regulations, & a lack of trained personnel impede scale-up, particularly smaller manufacturers who have low margins.(15)

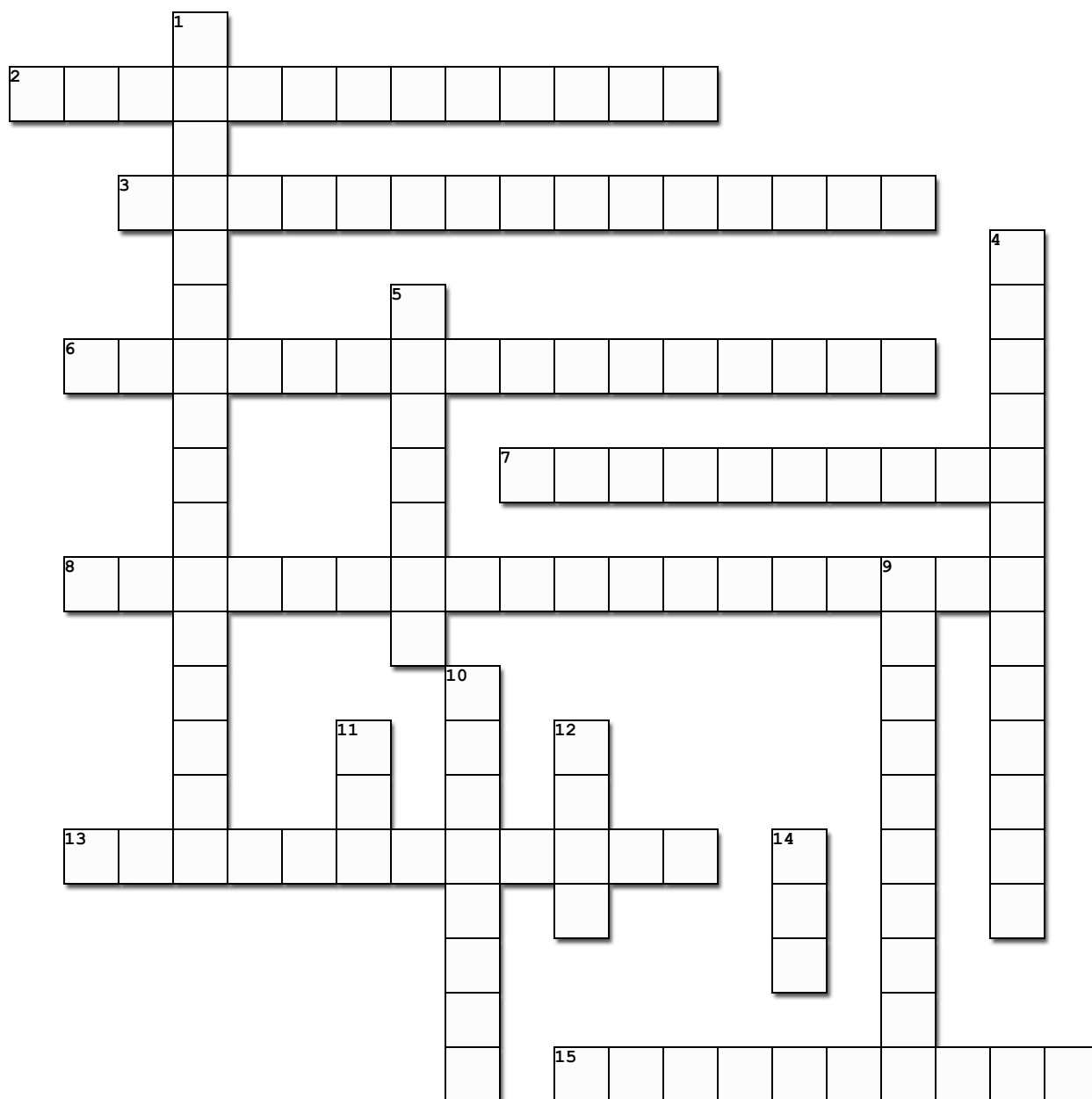
## 9. Conclusion

Sustainability in pharmaceutical industry is not a one-off initiative in a department but a part of the product life cycle. Design decisions ensure that entire process is both efficient & transparent. From API synthesis bench to use of LCA to inform design decisions, every step is efficient & transparent. From manufacturing & packaging design to collection & disposal at the end of their useful lives, medicines are essential for living. Medicines are vital to life from their manufacturing & packaging design to their collection & disposal at the end of their useful lives. A tangible opportunity to reduce environmental impacts without compromising the maintenance of life in the process is provided by life. Pharmaceutical industry is in the process of changing. In this context, towards a unified approach to sustainability, continuous manufacturing, mono-material & biodegradable plastics are gaining increased traction. The three solutions are all linked to bio-based packaging. The three solutions mentioned above are all related to bio-based packaging, coming together.

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Complete the crossword puzzle below

**Across**

- 2. Concept of biodegradable pharmaceuticals
- 3. Economy focusing on minimizing waste
- 6. sustainable alternative to reduce power consumption and waste
- 7. Plastic derived from renewable biological sources
- 8. Method to split complex aluminum-plastic blister foils
- 13. Packaging made primarily from a single material to facilitate recycling
- 15. Green pharma packaging

**Down**

- 1. creating medicines that safely break down in nature after use
- 4. Plant based packaging material
- 5. Digital Packaging
- 9. Recycling system that returns recovered materials to production
- 10. Structured medicine and device recovery scheme
- 11. Tool for Eco Design abbr
- 12. Eco-packaging innovation
- 14. Recyclable plastic abbr.