Advancing Sustainability in API Manufacturing
Practical Pathways for Energy and Materials Transition

By Joris Gilberts, Sustainability Manager
Aspen API, Oss, The Netherlands

Executive Summary
API manufacturing faces a dual sustainability challenge: decarbonizing energy systems and transitioning toward circular material flows. While sustainability includes broader goals, this paper focuses on API manufacturing's journey to net-zero emissions. The energy transition is technologically mature and ready for implementation, while the materials transition addresses upstream emissions and remains constrained by regulatory complexity and the limited availability of circular feedstocks.

A pragmatic approach balances ambition with feasibility, highlighting actions manufacturers can take today while preparing for a future in which green chemistry and circularity become industry norms. In the near term, meaningful progress is driven by a straightforward principle: consume less and recycle more. By reducing resource use, recovering solvents, and improving waste handling, companies can achieve measurable environmental gains while lowering operational costs. At the same time, long-term transformation — through upstream materials optimization, circular feedstocks, and new product design — is essential for achieving net-zero across the value chain.

Industry perspective from practice

This white paper reflects insights from Aspen API's experience across API manufacturing operations and engagement with customers, suppliers, and regulators, informed by Aspen API's active collaboration within industry bodies such as APIC, where it also contributes to and advocates for practical, sustainable manufacturing practices and the removal of systemic barriers.

Introduction: Sustainability Challenges in API Manufacturing

API manufacturing is resource intensive, energy demanding, and highly regulated. As expectations for climate action rise, pharmaceutical companies must demonstrate credible progress in reducing emissions, minimizing waste, and improving resource efficiency. While sustainability in the broad sense encompasses social responsibility, circularity, safety, and ethical sourcing, this paper focuses on **API manufacturing's journey to achieving net-zero emissions**. Achieving net-zero requires action both **onsite through energy decarbonization** and **across the value chain through the materials transition**. Optimizing materials — by reducing fossil-based feedstocks, recovering and recycling solvents, and adopting circular

inputs — addresses upstream carbon in purchased chemicals (Scope 3), which can often represent the largest share of an API's total footprint.

The broader pharmaceutical and biotech sector is estimated to contribute around 4–5% of global greenhouse gas emissions. Within this footprint, API manufacturing represents one of the most carbon-intensive stages of the value chain. Multiple lifecycle assessments show that API synthesis can account for 60–80% of the total cradle-to-gate emissions of a finished medicine, driven by energy-intensive synthesis routes, solvent use, and fossil-based chemical feedstocks. This places API manufacturers at the center of the sector's **net-zero decarbonization pathway**, even as other aspects of sustainability—such as social and material stewardship—remain important.

While this paper focuses primarily on site-level energy and materials use, a significant share of the environmental footprint of API manufacturing lies upstream in Scope 3 emissions, particularly in the production of solvents, reagents, and intermediates. Addressing these emissions requires stronger engagement with suppliers—through transparency on carbon footprints, shared expectations on greener materials, and collaboration on solvent recovery or circularity initiatives. Although the availability of low-carbon feedstocks remains limited, early supplier engagement helps prepare the ground for future circular supply chains.

At the same time, site-level improvements remain the most immediate and controllable levers for API manufacturers. Strengthening energy efficiency, optimizing solvent use, and improving waste management offer tangible benefits today, even as the industry works with suppliers to prepare the ground for future circular feedstocks.

This paper presents a realistic pathway for advancing **net-zero emissions** in API manufacturing across two complementary domains:

- **The energy transition**, which is technologically clear and ready for deployment.
- **The materials transition**, which addresses upstream carbon in purchased inputs and requires incremental progress toward circularity.

Pathways for Energy and Materials Transition

Energy Transition: Technologically Clear, Investment-Dependent

Among the sustainability challenges facing API manufacturing, the energy transition is the most straightforward. The technologies needed to decarbonize heating and cooling—industrial heat pumps, advanced cooling systems, electrified boilers, and integrated heat recovery concepts—are already proven in multiple industrial sectors. Their performance and reliability make them fully suitable for pharmaceutical environments.

A Holistic View of Thermal Energy

Leading companies increasingly adopt a holistic view of thermal energy flows. Instead of treating heating, cooling, and ventilation as isolated utilities, they map all thermal

streams across the site—process heat, waste heat, building heating, and cooling loads—and integrate them into a single optimized system. This approach often reveals opportunities to upgrade and reuse waste heat, supply heating and cooling simultaneously through heat pumps, and reduce overall energy consumption. Industries such as food processing, chemicals, and pulp & paper already use these integrated systems at scale, demonstrating their applicability to API manufacturing.

The Real Barrier: Investment and Timing

Despite the clarity of the technological roadmap, the main challenge lies in the high cost of the required investments and the timing of those investments. Many facilities lack the electrical infrastructure needed to support large heat pumps or electrified boilers, requiring substantial upgrades before new technologies can be installed. GMP critical utilities demand high reliability and redundancy, which can increase the complexity of integrating new systems. Retrofitting heat recovery concepts into existing buildings can be challenging when equipment layouts, pipe routing, or cleanroom constraints limit flexibility. These hurdles do not undermine the feasibility of the energy transition but require careful planning and phased execution.

Materials Transition: Complexity, Innovation, and Regulation

While the energy transition benefits from technological maturity, the materials transition is far more complex. API manufacturing relies heavily on fossil-derived chemicals, and the shift toward circular feedstocks is still in its infancy.

Heterogeneity of API Manufacturing

API manufacturing is not a uniform category. Energy intensity, solvent use, and waste profiles vary significantly between chemical synthesis, fermentation, and biotech-based processes. Even within small-molecule manufacturing, the sustainability levers differ between high-volume generics, low-volume specialty APIs, and early-stage clinical production.

Circular Roadmaps and Feedstock Limitations

Existing circularity roadmaps—such as the EU Circular Economy Action Plan, CEFIC's Transition Pathway, and the Plastics Europe Circularity Roadmap—focus primarily on plastics, packaging, and bulk chemicals, not the fine chemicals or pharmaceutical intermediates used in API manufacturing. Circular starting materials for specialty and fine chemicals are limited, inconsistent, and often unavailable at pharmaceutical-grade purity. Even circular solvents are limited to a small number of simple molecules and are often significantly more expensive than fossil-based equivalents.

Early signals of innovation exist: bio-based or recycled solvents such as bioethanol, recycled acetonitrile, or bio-based MEK are being piloted. Some chemical producers are experimenting with bio-based building blocks derived from lignin, sugars, or CO_2-based chemistry. These remain niche and not yet available at pharmaceutical grade or scale.

Regulatory Complexity as a Barrier

Even when greener materials or processes become technically viable, regulatory complexity is often a **larger barrier than commonly assumed**. Every API is typically registered across multiple markets, each with its own regulatory authorities, expectations, and timelines. A single change in solvent, raw material, or process condition can cascade into dozens of regulatory variations, requiring comparability data, stability studies, and updated risk assessments.

This burden is not merely administrative; it significantly influences decision-making by increasing cost, extending timelines, and introducing approval uncertainty. Emerging industry dialogue suggests that commercial priorities, including cost and supply considerations, influence how sustainability is weighed between API manufacturers and their customers, particularly when assessing material and process changes. As a result, many sustainability-driven improvements are delayed or deprioritized, even when their environmental benefits are clear.

Critically, this challenge cannot be solved by individual companies acting alone. Meaningful progress will require an **industry-wide approach**, including greater regulatory alignment, shared scientific justifications for greener materials, and coordinated engagement with authorities to establish risk-based, sustainability-enabling pathways.

Embedding Sustainability into Product Development

The APIs and processes being developed today will remain in production for decades. Early-stage design decisions therefore represent one of the most powerful levers for long-term sustainability.

AIPC's Safe and Sustainable by Design (SSbD) framework provides a structured method for integrating safety, environmental performance, and societal value from the earliest stages of product and process development. At its core, SSbD encourages companies to anticipate hazards, minimize resource use, and design processes that remain sustainable and compliant throughout their lifecycle.

However, time-to-market pressures often dominate early development. Companies must move quickly through clinical phases and secure market authorizations, which means sustainability principles are not always prioritized during route selection or early process design. Embedding SSbD into development workflows—while acknowledging real-world constraints—helps ensure that new products are designed with long-term sustainability, regulatory resilience, and resource efficiency in mind.

Practical Measures: Start Small, Act Now

Given the constraints of circular feedstocks and regulatory complexity, API manufacturers should focus on tangible, incremental improvements that deliver real environmental benefits without triggering major regulatory changes.

Consume Less, Recycle More

- **Use fewer resources:** Reducing energy consumption through targeted efficiency measures, minimizing water use via closed-loop systems, and optimizing processes to reduce chemical and solvent consumption.
- **Reuse and recycle:** Expanding solvent recovery, reusing process water, and integrating heat recovery systems reduces dependence on virgin materials and cuts waste disposal costs.
- **Separate waste streams:** Improving waste segregation, training operators in consistent waste handling, and collaborating with waste processors to identify new recycling pathways.

These practical measures enable meaningful progress today while complementing longer-term strategies that guide investment decisions, regulatory engagement, and capability building.

Strategic Recommendations for Near- and Long-Term Impact

Accelerating sustainability in API manufacturing requires both site-level action and industry-wide collaboration. While many of the measures outlined below can be initiated at site level, their full impact depends on coordinated engagement across the value chain, including suppliers, customers, and regulators. Individual companies can make progress through efficiency improvements, solvent recovery, and better waste management, but the full transition toward low-carbon and circular production will only be achieved if the sector works collectively.

Near-Term Priorities: Strengthen understanding of thermal energy flows, identify opportunities for heat and cold integration, expand solvent recovery, improve waste segregation, and embed green chemistry principles into R&D workflows.
Medium-Term Actions: Plan and execute investments in electrified utilities (heat pumps, advanced cooling systems), transition to low-carbon energy sources, pilot bio-based or recycled solvents, and develop structured regulatory strategies to enable incremental process improvements.
Long-Term Transformation: Reshape API manufacturing by adopting circular feedstocks as they become available, redesigning legacy processes for sustainability, and building electrified utility systems. Partnerships across chemical and pharmaceutical sectors are essential.

Leadership Grounded in Reality: Conclusions and Outlook

Sustainability offers API manufacturers a strategic opportunity to lead rather than follow. By piloting circular feedstocks and greener solvents, engaging in cross-industry initiatives, and collaborating with suppliers and regulators, companies can influence standards, accelerate adoption of low-carbon practices, and embed sustainability into product development. Early integration of Safe and Sustainable by Design (SSbD) principles ensures long-term environmental performance.

Leadership grounded in practical action—what effective thought leadership should represent—transforms sustainability from a compliance exercise into a competitive advantage, shaping the sector's trajectory and enabling meaningful differentiation.

However, translating ambition into impact requires acknowledging several structural realities:

- Current production processes — and even those in late-stage development — will remain in operation for decades and are not easily made circular.
- Most APIs are produced in multi-product facilities using energy-intensive and highly specialized processes that cannot be retrofitted quickly without major regulatory, operational, and financial implications.
- Even when greener feedstocks or solvents become available, regulatory hurdles, process validation requirements, and multi-market approvals make rapid adoption challenging.
- Circularity at scale will require decades of coordinated effort, making incremental, practical measures today — efficiency, reuse, waste segregation — critical for near-term impact.

Knowing how big the challenge is does not mean we can't take action now; strategies grounded in reality, combined with practical steps today and collaboration across the industry, build the foundation for long-term circularity and a low-carbon future.

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