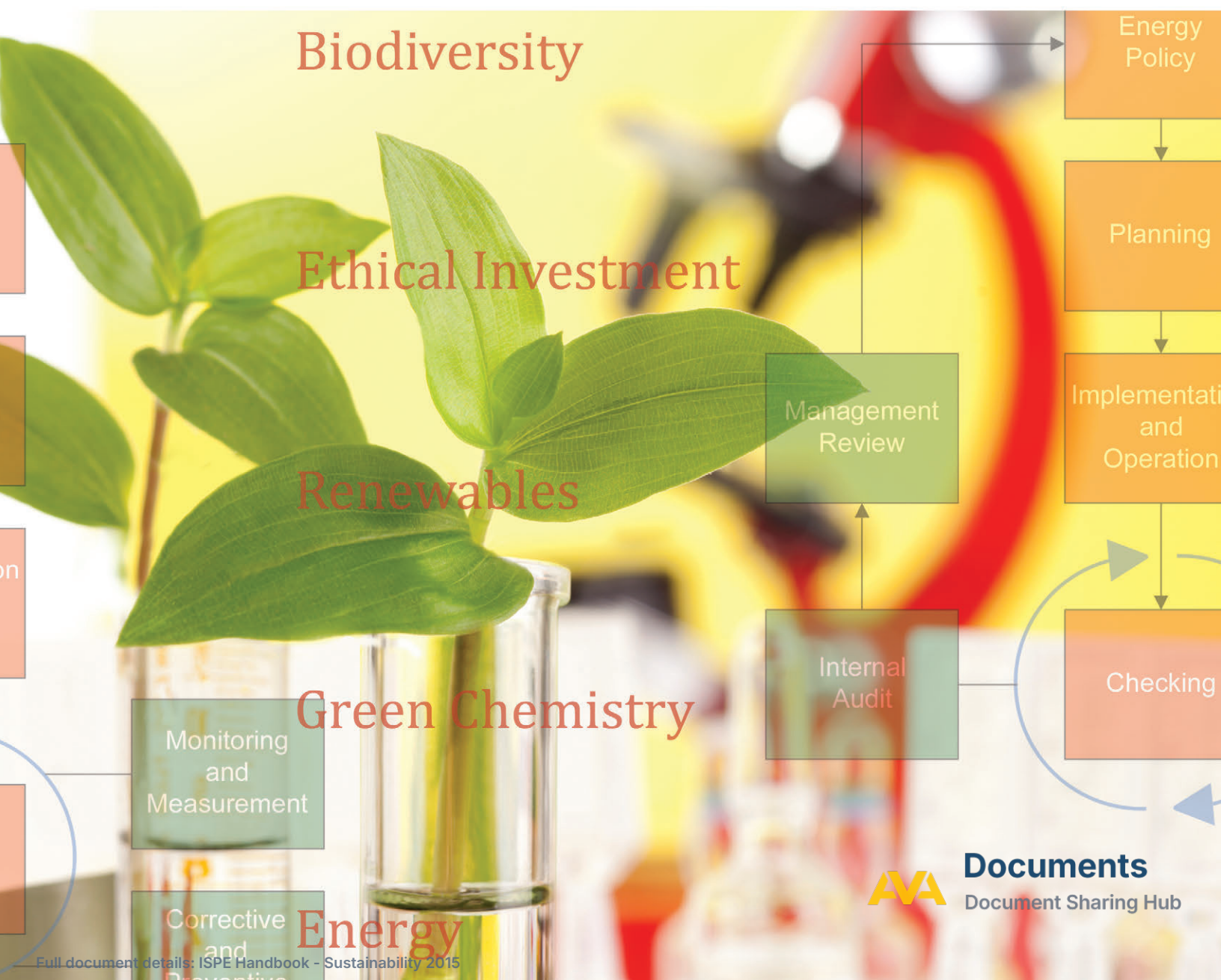


Sustainability Handbook





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This ISPE Handbook on Sustainability is intended to provide information at the front end of projects that will be useful to the project team in understanding sustainability and its associated criteria as applied to the life sciences industry, with examples where considered useful to explain or provide cause for thought. ISPE cannot ensure and does not warrant that a system managed in accordance with this Handbook will be acceptable to regulatory authorities. Further, this Handbook does not replace the need for hiring professional engineers or technicians.

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Preface

The *ISPE Handbook: Sustainability* considers sustainability in the context of our life sciences industry, although much of the content is relevant to any industry. It is the first handbook of its type rather than Baseline® Guide or Good Practice Guide that has been published by ISPE.

As an updatable source book with typical guidance in each of the key topic areas rather than set of a definitive guidance items it has been designed to be improved as new information, methods and technologies present themselves.

There are two key sections: Principles/Policy and Design/Engineering application. The first is about what sustainability is, legislative and regulatory impacts, and guidance on sustainability policy making. The second considers the impact of and provides indicative guidance on sustainable drug process and manufacture from facility location and design to equipment selection and use.

Who it is for: A broad spectrum from board to operations/facility manager; from project manager through design engineer and architect to site based equipment engineer as a flick through, pause-and-find tool in the resolution of a better way.

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The Handbook was produced by a Task Team led by Robert J.E. Bowen (Facilities Integration Ltd.) and Nicholas Haycocks (Amgen Inc.). The work was supported by the ISPE HVAC and Sustainable Facilities Communities of Practice (COP).

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Company affiliations are as of the final draft of the Handbook.



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Part 1

Principles/Policy

1 Introduction

1.1 Background

Sustainability, or sustainable development, is defined as:

“Development that meets the needs of the present without compromising the ability of future generations to meet their own needs.” [1]

Sustainability, and particularly reference to climate change, is considered by some to be contentious. The authors of this handbook have based their definitions and premises on those adopted and accepted by the United Nations, which in turn refers the Intergovernmental Panel on Climate Change (IPCC) for its scientific guidance. The IPCC [2] was established by the United Nations Environmental Programme and the World Meteorological Organisation in 1988. The climate change element of the world congress is coordinated through the United Nations Framework Convention on Climate Change (UNFCCC) [3].

Figure 1.1: Defining Sustainability

Courtesy of Indiana University Office of Sustainability; adaptation of public domain depictions of the Triple Bottom Line.



Sustainability, or rather what are considered as sustainable solutions – have, to date, been accepted in practice where there are obvious commercial benefits when applied to existing systems. Many, if not most, pharmaceutical companies have accepted initiatives that provide potentially significant reductions in risk, such as, where considered viable, the introduction of green chemicals, reductions in air volumes and use of off-the-shelf photovoltaics.

What may not be quite so apparent is that, once accepted as a principle, sustainability as a philosophy may provide overall gains industry wide with improved public perception and company and staff pride in being members of a responsive and responsible life sciences and health care industry.

It is suggested that sustainable development is adopted as an industry baseline with a set of key performance criteria set in line with, or ahead of, the current highest legislated standard and reflected through the calculated environmental assessment performance of a facility, based on such as:

- Leadership in Energy & Environmental Design (LEED) Platinum [4]
- Building Research Establishment Environmental Assessment Methodology (BREEAM®) Excellent or Outstanding [5]

- An equivalent assessment level in a similarly approved environmental assessment methodology

It is also suggested that Life Cycle Assessment (LCA), also based on an approved set of principles/software bases, is generally adopted by our industry.

1.2 Why do we need this Handbook?

The principle of sustainability, or more correctly, sustainable development (see Figure 1.1), has existed as long as humankind has existed. Maintaining “the capacity to endure” [6] has been the abiding focus of us as tribes, as farming communities, and as industrial entities. In current phrasing, “sustainability” refers to the wide range of measures considered necessary to help avert issues associated with climate change such as hemispheric temperature change (see Figure 1.2), the increasing world population, (see Figure 1.3), and the effects of carbon dioxide (CO₂) and other greenhouse gases on the atmosphere (see Figure 2.1). Other practices that support the same goal include eco-friendly design and its consideration of the impact of materials and facilities on a pharmaceutical site’s biodiversity.

Figure 1.2: Annual Mean Temperature Change for Hemispheres

Source: NASA Goddard Institute for Space Studies, January 2013 update.

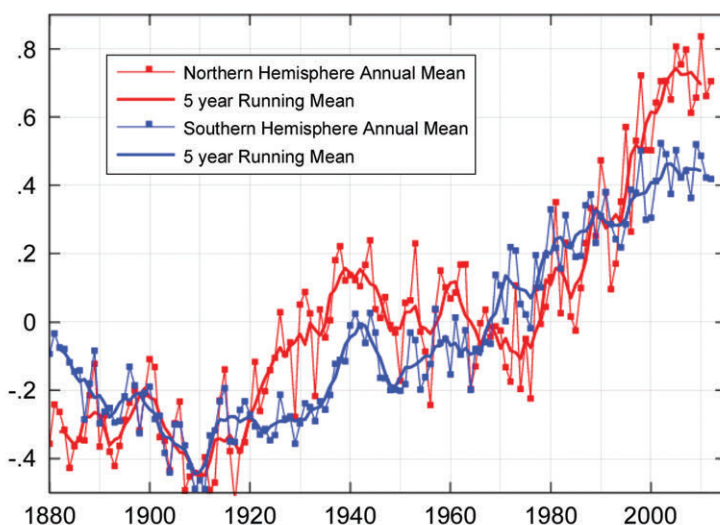
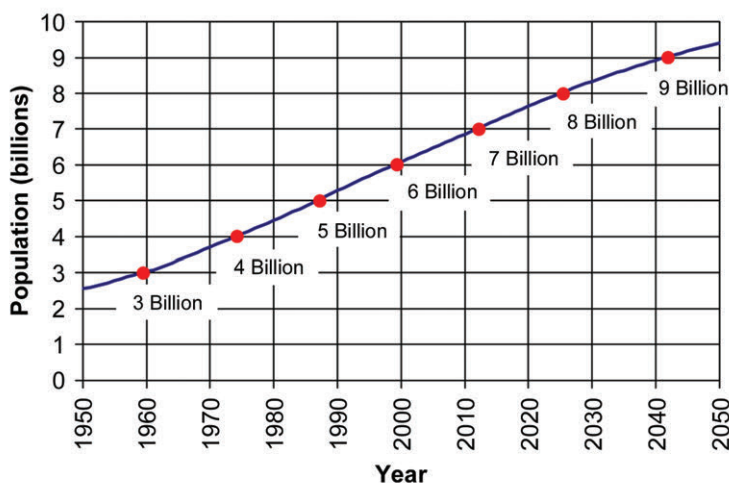


Figure 1.3: World Population 1950-2050

Source: US Census Bureau International Database, July 2015 update.



The handbook has been written around the premise that there is a viable path to achieving sustainability that corresponds to all of the precepts of the life sciences industry. This is an especially important ethical consideration for the health care industry, which has a focus centered on maintaining or improving the health of the patient.

This handbook is written to provide information at the front end of projects that will be useful to the project team in understanding sustainability criteria, with examples where considered useful.

1.2.1 *Relationship to Other ISPE Guidance*

This handbook is intended to act as a reference to provide information that may be useful in the development of new projects, e.g., greenfield, brownfield, or retrofits. It is intended to complement ISPE Baseline® and Good Practice Guides. The intention is to review and update this handbook in relation to other ISPE guidance on a regular basis to ensure cross-compatibility and information alignment.

Contextual Concerns

A decision should be made to determine whether the measure of success is purely financial, or whether there is a sustainability dimension, such as direct or indirect CO₂ release. This should be part of project decision making during the start of the design of new facilities or systems, or the upgrading and improvement of existing facilities. The decision may be influenced by an organization's green credentials and corporate sustainability profile. If CO₂ is the main focus, then outcomes may be based on the varying levels of CO₂ released from electrical grid power generation.

The main influencing factors are the:

- Energy source or sources for power generation
- Efficiency of generation
- Losses in distribution

In much of northern Europe, electrical power is generated through a combination of some renewables, oil, gas, coal, and nuclear. In this region, it is common to see a CO₂ release per kilowatt hour (kWh) of electricity of 0.5 to 0.6 kg/kWh. In a region where there is much greater influence of nuclear power, then the CO₂ release is closer to 0.2 kg/kWh. This is a significant difference. Where electrical power generation is dominated by coal-fired power stations and long power transmission distances, e.g., in Australia or China, values of CO₂ release of more than 2 kg/kWh are frequent.

The choice for a site's location may be different if it is determined by a CO₂ emission based decision, rather than purely by a financial, political, or market based decision (see Appendix 1).

1.3 **Objectives**

The key objectives of this guide are to:

- Provide a reference point for sustainability in the life sciences industry for project teams
- Provide a global pharmaceutical sustainability baseline for the life sciences industry through promotion of the reduction of consumption of finite resources and consideration of the effects of environmental shifts
- Respect the industry's advanced engineering traditions by providing an informative and easy to use document. Directions of research for project teams are given in each of the engineering areas from product development through to facility development.

- Provide a route map to understanding the legislative conditions worldwide that either exist at the time of writing or are understood to be in progress
- Promote the development of sustainability policies and guidelines that apply to specific organizational needs

1.4 Key Terms

A glossary is included in Appendix 5. Some terms are explained here and should be understood prior to reading the main content of this handbook.

Biodiversity: Biodiversity is the reference to ensuring retention of the balance of nature through any development or act. Examples include ensuring that a development does not affect a finite resource or upset the home of a species without due consideration of its capacity to survive in continuum.

Carbon Footprint: A carbon footprint measures the total greenhouse gas emissions caused directly and indirectly by a person, organization, event or product. *“A carbon footprint is measured in tonnes of carbon dioxide equivalent (tCO₂e). The carbon dioxide equivalent (CO₂e) allows the different greenhouse gases to be compared on a like-for-like basis relative to one unit of CO₂. CO₂e is calculated by multiplying the emissions of each of the six greenhouse gases by its 100 year global warming potential (GWP).”* [7] Also see **Greenhouse Gases**.

Carbon (Emissions) Trading: Emissions, or carbon, trading, as set out in Article 17 of the Kyoto Protocol, allows countries that have emission units permitted them that are not “used” to be traded to countries that are over their targets. Carbon credits (one credit = one metric tonne of CO₂), or emissions permits, are available to trade also through domestic or regional emissions trading schemes working to overall nationally set targets, (UNFCCC International Emissions Trading [8]). Also see **Greenhouse Gases**.

Embedded (Embodied) Carbon or Energy: *“[T]he sum of all the energy required to produce any goods or services”* and *“an accounting method which aims to find the sum total of the energy necessary for an entire product life cycle.”* [9] This includes tracing the source of materials and ensuring that the carbon footprint is within reasonable bounds. *“[T]he emission of energy-related pollutants, like CO₂, which is a concern in the context of global warming and climate change, may be viewed over their life cycle. This gives rise to the notion of ‘embodied carbon’.”* [10] Also see **Carbon Footprint**.

Ethical Investment: *“Investment philosophy which attempts to balance the regard for morality of a firm’s activities and regard for return on investment. Ethical investors seek to invest (usually through mutual funds or unit trusts) in firms which make a positive contribution to the quality of environment and quality of life.”* [11]

Green (Sustainable) Chemistry: The design of chemical products and processes that reduce or eliminate the generation of hazardous substances [12].

Greenhouse Effect: *“Greenhouse gases effectively absorb infrared radiation, emitted by the Earth’s surface, by the atmosphere itself due to the same gases, and by clouds. Atmospheric radiation is emitted to all sides, including downward to the Earth’s surface. Thus greenhouse gases trap heat within the surface-troposphere system. This is called the natural greenhouse effect.*

Atmospheric radiation is strongly coupled to the temperature of the level at which it is emitted. In the troposphere the temperature generally decreases with height. Effectively, infrared radiation emitted to space originates from an altitude with a temperature of, on average, -19°C, in balance with the net incoming solar radiation, whereas the Earth’s surface is kept at a much higher temperature of, on average, +14°C.

An increase in the concentration of greenhouse gases leads to an increased infrared opacity of the atmosphere, and therefore to an effective radiation into space from a higher altitude at a lower temperature. This causes a radiative forcing, an imbalance that can only be compensated for by an increase of the temperature of the surface-troposphere system. This is the enhanced greenhouse effect.” [13]

The effect of this on climate change is known to be a matter of argument with both believers and disbelievers. The prevalent world view is that climate change with the greenhouse gas effect as a major contributor is accepted as a theory rather than a hypothesis. Also see **Greenhouse Gases**.

Greenhouse Gases: The Kyoto Protocol greenhouse gases are carbon dioxide (CO₂), methane (CH₄), nitrous oxide (N₂O), hydrofluorocarbons (HFCs), perfluorocarbons (PFCs) and sulfur hexafluoride (SF₆). These are those gases that, if imbalanced, are considered to be detrimental to the Earth’s own environmental performance via the “greenhouse effect”.

Renewables: The use of a method of energy production that is obtained from a renewable source. Examples of renewable sources include power obtained from wind, water, solar or geotechnical resources.

Sustainable Chemistry: see **Green Chemistry**.

Sustainable Practice: Adopting a course that is considered sustainable. Following an ethical design path that includes consideration of, e.g., masterplan review of existing sites and practices, and setting a course based on provision of sustainable outcomes.

Sustainability (Sustainable Development): *“Development that meets the needs of the present without compromising the ability of future generations to meet their own needs.” [1] “It is simple, really. Human health and the health of ecosystems are inseparable.” [14]*

¹ Gro Harlem Brundtland: Prime minister Minister of Norway (1981, 1986-1989, and 1990-1996) and director general of the World Health Organization (1998-2003).

2 Sustainability in the Context of the Life Sciences Industry

2.1 Introduction

This guidance is intended to provide an opportunity for improvement in operational methodologies, quality, simpler and safer material handling, a clearer conscience and an improved bottom line. Inevitably there are challenges to current practices that may go against a locally accepted condition. It is suggested that where this occurs the project is reviewed on a holistic basis and either a current condition accepted or proposals made for sustainable improvements. Good sustainable design can provide a positive return on investment and ensure reductions in operational overhead that will reflect in a favorable cost of goods.

2.2 Relevance to Latitude/Hemisphere

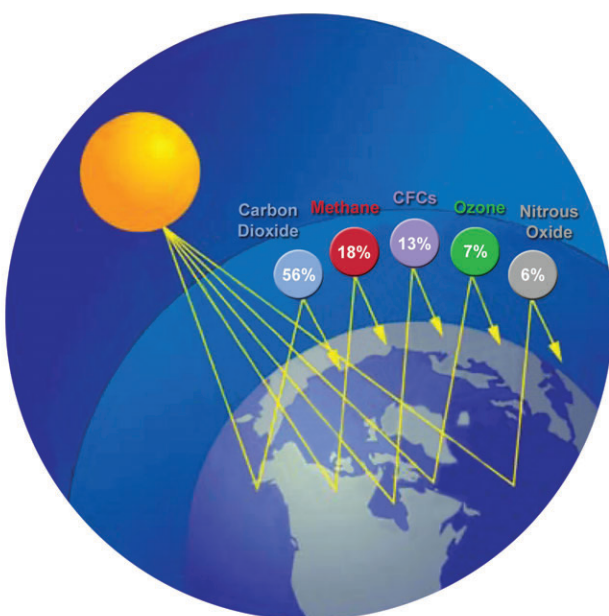
The effects of sustainable development differ for different regions of the world, affecting locations on a macro, local and micro basis. Siting a facility:

- In an arctic location will differ from siting one in an equatorial location
- In temperate latitudes will differ from siting one in Mediterranean climate zones
- On a seismic zone will differ from siting one on a flood plain

Each of these factors will lead to specific conditions needing to be met in the risk profile, building format, cultural, and climatic response. Personnel at facilities in locations with a seemingly constant climatic condition may tend not to feel that there is any change to respond to as all is well, locally. Where climatic changes are being felt, personnel are likely to have a more strident view of that aspect of sustainability.

Figure 2.1: Greenhouse Gases

Courtesy of the Marian Koshland Science Museum of the National Academy of Sciences. Copyright © 2015 National Academy of Sciences. All rights reserved.



2.2.1 **Broad Issues**

There is reasonable proof that resources are declining and are finite; a simple pharmaceutical example being the potential risk of depletion in availability of the inert gas helium. Populations are increasing, generally disproportionately, and using increasing amounts of finite resources. While new methods make extraction of previously considered unavailable resources – such as coal – financially viable, this only postpones the inevitable. Sensible resource management has become a necessity.

2.2.2 **The Business Case**

The business case for involvement in sustainability is becoming increasingly attractive as time passes and the cost options become more transparent [15]. In addition the countries that have adopted sustainable principles are introducing legislation that enforces sustainable practices. In addition, shareholder concerns, the availability of ethical investment funding and intellectual worker expectation/satisfaction all figure in making engagement worthwhile, and in some cases, unavoidable.

2.2.3 **Ethical Investment**

There has been a notable rise in ethical consumerism, even during the world recession of the first decade of the second millennium. The expectation of purity of source and ethical validity of a product, whether that is shares in a company or the final product, is increasingly capturing the attention of potential consumers. A preparedness to pay more for or demand a product that is not following the cheapest route is apparent.

2.2.4 **How does this affect the life sciences industry?**

The worldwide recession brought with it changes in company fortunes that, when mixed with an ongoing rebalancing of global wealth and a decline in the product pipeline, have combined to pose significant challenges to traditional life sciences companies (i.e., “big pharma”). They have been further challenged by generic manufacturers and contract manufacturing organizations, as products come off patent, making a focus on the cost of goods inevitable. This has affected Oral Solid Dosage (OSD) products for some time and now includes challenges to biosimilars. In addition, new product is emerging that is developed in different forms and by significantly different means than the Active Pharmaceutical Ingredient (API)/chemical excipient processes of “traditional” chemical based products. Similarly, advances in capability to increase titer mean that the biologics manufacturers have the opportunity to rethink their manufacturing processes.

Development costs and the prohibitive nature of the effort and expense in relicensing products mean that changes in process come at a price that may not immediately be considered worthy of commercial consideration. This has stood as a barrier to new development.

Sustainable options are often difficult to achieve in facilities that use equipment and chemical formulae or biological setups that may date back 100 years.

There is an opportunity for the industry to take a leading role in the ongoing science, technology and sustainability revolution available through developments both within this industry and transferred from other industries. These developments can provide significantly greater operational flexibility than that available through traditional laboratories or batch manufacture. They can also provide the opportunity for significant sustainable cost gains throughout the process. Opportunities include:

- New principles of chemical design for manufacture through the use of Quality by Design (QbD) principles
- New materials and manufacturing methods that make process closure and/or continuous operation more accessible, e.g.:

- Smart engineered plastics as metal replacements providing smarter, simplified valving systems and smooth biosafe connections
- Improved equipment production techniques and design practices, which provide more ergonomic interfaces and safer accessibility
- Integration of smarter isolation systems, which allow system closure as a secondary or tertiary containment, reducing the need for additional room containment
- Increased automation and robotic options, when linked with process analytical technology (PAT) identification and characterization, which allow rapid, controlled, quality assured transfer of product from one process stage to another
- Smaller, modular, flexible equipment setups and rigs, which provide opportunities for changes in location and new operational paradigms
- Smarter and more visible control systems, which allow more portable interfaces
- An enlightened approach to operations through the availability of additional metrics and quotas, e.g., an energy or emissions budget in kWh or CO₂

Many of the new materials and manufacturing methods are accessible to all stages of drug development from the Research and Development (R&D) laboratory through to warehousing and packaging operations, providing a more sustainable approach.

There is always a cost to transition into new technologies, but engaging with a more sustainable approach to design, implementation, and operation is now feasible, available, and increasingly necessary, particularly when linked to a more open risk-based regulatory environment and new sustainability-based parties to whom organizations are accountable. Some of the sustainability based parties are voluntary, such as rating system reviewers and internal corporate sustainability managers; others are mandatory, such as regulators and energy code officials.

2.2.5 *What does that mean in engineering and architectural terms?*

Designers and engineers of systems, as operational engineers and architects involved in pharmaceutical process and facility design, engineering and maintenance, are members of a global industry that needs to respond to the commercial pressures of drug discovery, development and production.

The choices are whether to achieve sustainability by legislative default, or engage up front in ensuring that significant improvements are achieved. Throughout the Drug Product (DP) supply chain, use of sustainable options provides overall gain. Example areas of engagement addressed in this handbook include:

- Working with company boards in setting a sustainability policy:
 - Developing a route-map
 - Providing resources
 - Promoting initiatives
 - Measuring outcomes
 - Costing Return on Investment (ROI)
 - Rewarding success

- Applying environmental management standards, e.g.:
 - ISO 14001:2015 [16]
 - ISO 50001:2011 [17]
- Reducing carbon take through:
 - Carbon footprinting
 - Tracing embodied carbon
 - Using renewable energy production resources
 - Changing boiler systems to eco-friendly fuels
 - Consideration of modes of transport
- Reducing solvent reliance:
 - Using green chemistry solutions where possible in development of new processes
 - Challenging and reformulating existing products and processes
- Reduction in use of energy through:
 - Reducing airflows and room backgrounds
 - Greater use of air recycling
 - Increased use of isolation techniques
- Adopting a “no waste” philosophy:
 - Considering all options for recycling both internally or through fair market means from water and chemicals to packaging and stationery
- Considering water usage and quality through:
 - Adoption of ISO 6107 series [18]
 - Adoption of recycling process water rather than once through
 - Use of greywater
 - Use of ground absorption techniques
- Improve insulation of facilities and equipment more efficiently to maintain product viability and comfort environments through:
 - Challenging the heat output of processes
 - Use of smart heat exchange techniques and phase change materials

- Re-use of available heat and cooling efficiently and effectively
- Challenging the supply chain methodology by:
 - Reducing warehousing to required storage
 - Reducing process steps and quarantining, where possible

Sustainability initiatives may contradict the established norm, but with team engagement viable, cost-effective solutions may be found that retain customary expectations of secure and safe operation even in the rigid operations required of, e.g., API or steriles production. Such initiatives can provide significantly more cost-effective means of production.

In the design of new facilities and the retrofitting of existing ones, using Building Information Modeling (BIM) [19] linked with environmental review tools provides the opportunity to include sustainability into each of the review processes to ensure that holistically sustainable solutions are captured and the opportunities are acted upon.

Sustainable solutions are developing from advanced holistic thought and development of systems to provide significant benefits to the industry and, ultimately, patients.

3 Legislation

3.1 Introduction

The effect of legislation for the life sciences industry differs dependent on whether the organization involved is a global corporate organization or a nationally based organization. Finding the lowest-cost location for a global corporation involves both a cost objective and an added ethical factor.

Compliance with sustainability based legislation in some countries inevitably involves more capital expenditure, although it may be argued that over a long period this is recouped. Proving cost-effectiveness at initiation can be an issue because many of the results of the changes to achieve sustainable facilities will not be readily apparent other than through long-term investment, and additional investment may be required to achieve long-term gain.

3.2 Legislative Engagement

The medium of legislation is considered the most powerful pressure that can be applied to ensure closure on what would be otherwise a preference or desire. With a topic like sustainability, political will is needed for closure and engagement as, at least initially, achieving sustainable solutions or outcomes can cost money that commercially may not appear viable without either a direct lower cost or a preexisting infrastructure that is designed to accommodate a specific need, e.g., a viable recycling industry.

The danger for regions is that the more onerous they make legislation, the less likely it is that the corporates, (the most significant force in the industry), will wish to invest, unless there is any other incentive, or unless, of course, the market is too large to resist and the import burdens likewise too onerous; so there is a balance to be struck.

USA

Despite the reluctance to get involved with the Kyoto Protocol, the Energy Policy Act of 2005 [20] and the Energy Independence and Security Act of 2007 [21] include energy efficiency and sustainable design requirements for Federal and other buildings, additionally, there have been a series of executive orders and agency-specific rules promoting green building since the early 1990s and the federal government has instituted sustainable practices at many of its buildings [22]. The federal bodies, the Environmental Protection Agency (EPA) and the Office of Energy Efficiency and Renewable Energy (EERE) generally promote sustainable options. The EERE Advanced Manufacturing Office partners, with industry, small business, universities, regional entities, and other stakeholders to identify and invest in emerging technologies with the potential to “enhance global competitiveness and reduce energy use by encouraging a culture of continuous improvement in corporate energy management” [23].

Signed on 19 March 2015, Executive Order 13693 “Planning for Federal Sustainability in the Next Decade” [24] mandates that increasing percentages of energy for federal building be generated by clean technologies beginning in 2016.

European Union

Having accepted Kyoto in its entirety, the European Union (EU) imposed legislation on its member states. Singapore and Australia also applied early legislative nooses; Singapore’s case successfully balancing it against a low corporate tax profile.

The EU applied what is known as the 20-20-20 target through three key directives:

1. 2002/91/EC Energy Performance in Buildings Directive (EPBD). This originating directive was subsequently recast and upgraded as 2010/31/EU [25]

2. 2003/87/EC: Establishing a Scheme for Greenhouse Gas Emission Allowance Trading (see Section 3.3) [26]
3. 2009/28/EC: Promotion of the Use of Energy from Renewable Sources [27]

The three 20s refer to a:

- 20% cut in emissions of greenhouse gases by 2020, compared with 1990 levels
- 20% increase in the share of renewables in the energy mix
- 20% cut in energy consumption

In building terms the EPBD applies these reductions through requiring achievement of minimum energy performance standards for new and large refurbished buildings using an energy performance calculation methodology and expecting displayed energy certification. The directive also expects third party inspections of air conditioning systems and boilers on a regular basis to ensure their efficiency. In renewables terms each member country is required to respond to set performance targets for renewables based energy provision. The latest of the EPBD upgrade (2010/31/EU, referred above) tightens the squeeze on nations with an expectation of a near zero carbon target for new buildings by 31 December 2020 amongst other provisions [28].

UK (EU Example)

As an example, to achieve the EU expectations the UK legislates and controls on three fronts, legislation, regulation and monitoring. Changes of government and the world recession have had their affect in terms of method, but the target remains and the government of the day is assessed by an impartial committee – the Committee on Climate Change – that has specific annual reporting criteria. The accompanying legislation ensures that companies must report on energy usage and conform to both planning and building control (building quality) legislation and codes.

This is related to new construction and retrofitting of buildings and does not directly affect the manufacturing processes. These in legislation terms, again taking the EU UK model, are based on a carrot and stick approach when it comes to sustainability, primarily focused on energy reduction and renewables. The current UK primary industry incentivization tool is the Renewable Heat Incentive (RHI) which aims to provide a long-term financial incentive. The objective of the RHI is to significantly increase the proportion of heat generated from renewable sources by providing a tariff based subsidy, payable for 20 years, to eligible renewable heat generators [29].

Planning Code Controls

The quality of planning code, generally defined as legislation that expects local approval to the principle, siting, and visual design of a project, inevitably depends on the maturity of the nation, its legislative environment and its political will to implement legislation once it is passed. In this respect there is a responsibility on an ethical basis to consider whether the baseline is good enough.

Continuing with the EU based UK example, planning codes are obligatory and are required to conform to specific legislated mandatory criteria and policies. These are applied by the local authorities (equivalent to state/county or province) and work on a top down, ground up basis politically using local plans conforming to national criteria with specific national (federal equivalent) agencies looking after, e.g., environmental and highways matters. Any application whether green, brownfield, or retrofit must comply. Local authorities are required to expect environmental assessments (see Section 3.6 for environmental (EIA) expectations) and interaction with the government agencies responsible for environmental matters. These include 1:200/1:1,000 year flood attenuation, biodiversity response, finance for green transport projects, car and bicycle provision, and sustainable construction.

3.2.1 Cleanliness

The pharmaceutical issue most affecting being able to respond to sustainable objectives has been driven by the need to maintain clean backgrounds around open processes, maintaining high volumes of clean air backgrounds driving often a demand for increasing air changes with even greater volumes of 100% clean air through-flow. The restriction of passing air through HEPA filters inevitably drives the need for powerful drive motors using more energy, in turn taking up large plant spaces and needing significant duct sizes and service spaces, all of which lead to greater heat losses, responding building volumes and large boiler sizes.

The incapacity to do anything other than respond to a set of strictly regulated cleanroom containment rules has meant that meeting the low carbon objectives that are placed by those countries that have legislation expecting reductions has been almost impossible. Plant steam-based systems have meant that expected boiler efficiencies cannot be achieved.

The pharmaceutical industry is catching up to other industries in achieving sustainability objectives and needing to seek exemptions, which can be costly to implement.

Building Quality Code Controls

Continuing the UK example: Mandatory building regulations, which control build quality and performance, have been tightened over 3-year periods to achieve the required EU target carbon take through expectation. On application, each project must submit a mandatory Simplified Building Energy Model (SBEM) – a government approved third party energy use assessment method – to show a required partial renewables response that includes pressure testing of non-domestic (industrial) buildings and provision of energy performance certificates. The SBEM assessment must be proven on completion. This affects all new construction, including retrofits. Retrofits over 1,000 m² (approximately 10,000 sq ft) – it is anticipated that this will be reduced over time – attract scrutiny of the rest of the facility with an expectation of upgrades to a particular level to meet energy reduction criteria.

3.2.2 Waste Legislation and Regulations

The treatment, disposal, and transport of waste is determined predominantly by national legislation, but is also regulated at the local level. In addition, a number of comprehensive international regulations and guidelines exist, which offer considerations and definitions for various wastes and pollutants.

3.2.2.1 International Waste Guidelines, Treaties, and Regulations

On an international level, the following guidelines and regulations touch the scope of waste management in pharmaceutical manufacturing:

- World Health Organization (WHO) Safe Management of Wastes from Health-Care Activities [30]
- United Nations Environment Programme (UNEP) Waste Management Guidelines [31]
- Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal [32]
- Stockholm Convention on Persistent Organic Pollutants [33]
- Montreal Protocol on Substances That Deplete the Ozone Layer [34]

The European Union furthermore adopted an array of regulations and directives, which are partly of significant global relevance. Among them are:

- Regulation (EC) 1907/2006: Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) [35]
- Directive 2001/83/EC: Community Code Relating to Medicinal Products for Human Use [36]

- Directive 2010/75/EU: Industrial Emissions (Integrated Pollution Prevention and Control) [37]
- Directive 2008/98/EC: Waste and Repealing Certain Directives [38]
- Directive 2000/76/EC: Incineration of Waste [39]
- Directive 1999/31/EC: Landfill of Waste [40]
- Directive 1999/13/EC: Limitation of Emissions of Volatile Organic Compounds due to the Use of Organic Solvents in Certain Activities and Installations [41]

In the US, the EPA has put in place regulations that govern the disposal and treatment of waste. Among them are:

- Resource Conservation and Recovery Act (RCRA) [42]
- Spill Prevention, Control, and Countermeasure Plans (SPCC) [43]

In addition, various US institutions cover pharmaceutical manufacturing aspects, among them are:

- National Institute for Occupational Safety and Health
- Occupational Safety and Health
- Department of Transportation
- Food and Drug Administration (FDA)
- Drug Enforcement Administration

3.3 Carbon Trading Schemes

European Union

The largest trading scheme (2014) is the European Union Emissions Trading System (EU ETS); EU Directive 2003/87/EC [26] – empowered since 23 October 2003, and described as “the cornerstone of the European Union’s policy to combat climate change and its key tool for reducing industrial greenhouse gas emissions cost-effectively” [44]. This works on a “cap and trade” principle, as do most schemes. A cap is set on the total amount of greenhouse gases that can be emitted by all participating parties. “Allowances” for emissions are then auctioned off or allocated for free, and can subsequently be traded. In the EU ETS’s first year, 362 million tonnes of CO₂ were traded on the market for a sum of €7.2 billion, along with a large number of futures and options. Much like a stock market, companies and private individuals can trade through brokers who are listed on the exchange [44].

United States

In the US the Environmental Protection Agency (EPA), a federal body, has been administering cap and trade schemes since 1995 including the Acid Rain Scheme and the NO_x Budget Trading Program [45]. The Clean Air Interstate Rule (CAIR)² was launched in 2005 aimed at reducing power plant pollution. California has had a greenhouse gas reporting requirement in place since 2008, and launched a unilateral carbon trading scheme in 2012 commencing in January 2013 aimed at reducing greenhouse gases to 1990 levels by 2020 and ultimately achieving an 80% reduction from 1990 levels by 2050.

² Replaced by Cross-State Air Pollution Rule (CSAPR) [46].

China

China will have seven pilot carbon trading schemes. These are in Shenzhen, Beijing, Shanghai, Guangdong, Tianjin, Chongqing and Hubei, with the intention of it being taken nationwide in 2015/16 [47]. A national carbon trading scheme is to be introduced in 2017 [48].

3.4 The Place of Assessment and Life Cycle

In legislation and regulatory terms there are locations where there is an expectation for the application of environmental or life cycle assessment.

The EU, through its top down approach to achieving sustainability throughout the Union, has applied both the Environmental Impact Directive [49] and its three amendments; and the Strategic Environmental Assessment Directive [50] to require EU nations to assess, provide, and expect environmental screening of certain projects via the submission of environmental impact assessments and strategic environmental assessments (SEAs), with applications for pharmaceutical production facilities with a floor area in excess of 1,000 m² (approximately 10,000 sq ft).

Both the United States and United Kingdom expect all new government-associated buildings to be environmentally assessed. All new US federal buildings or major renovations, including those for lease, must meet LEED Silver or two Green Globes standards [51, 52]. The UK expects BREEAM "Excellent" certification for new buildings and "Very Good" for refurbishments for government-owned buildings.

Some UK local authorities expect BREEAM environmental assessments as a part of acceptance of a planning application.

Figure 3.1: Legal Requirements – Overview

WORLD	USA (example)	EU (example)	UK (example)	
2050 TARGET REDUCTION IN CARBON EMISSIONS BY 80% (1990) TARGET 15% POWER FROM RENEWABLES		EU TARGET 40%<2010 LEVELS	UK 2050 TARGET 80%<1990 LEVELS	2050
2040				2040
2030 TARGET REDUCTION IN CARBON EMISSION BY >24% ON 1990 LEVELS	2030 REDUCE CARBON POLLUTION BY 38% TONNES 2030 TARGET EXISTING POWER PLANTS EMISSIONS 30%<2005 LEVELS 2030 EISA TARGET FOR ENERGY INDEPENDENCE IN FEDERAL BUILDING STOCK 2025 TARGET 24-28% EMISSION<2005 LEVELS	2030 ENERGY EFFICIENCY TARGET 27%<PROJECTED 2030 EU GHG TARGET OF MIN 40%		2030
2020	2015 PARIS PROTOCOL: AGREEMENT TO 2020-2050 TARGETS 2012 KYOTO OBJECTIVE: 8% REDUCTION IN CARBON EMISSIONS (1990) 2009 COPINHAGEN PROTOCOL 2009 GB L'AQUILA - USA JOINS IN - 2050 TARGETS SET 2008 INTERNATIONAL YEAR OF PLANET EARTH 2007 AUSTRALIA RATIFIES KYOTO	2020 LARGE SCALE FACILITIES TARGET 21%<2005 2020 RENEWABLES TARGET 20% 2020 ENERGY EFFICIENCY TARGET 20%<PROJECTED	UK INTERIM TARGET 34% REDUCTION IN EMISSIONS<1990 SCOTLAND 42% REDUCTION IN EMISSIONS<1990 2019 ALL NEW NON-DOMESTIC BUILDINGS ZERO CARBON 2014 INCREASED ENVIRONMENTAL OFFENCE FINES 2013 CARBON EMISSIONS IN ANNUAL REPORTS OF LISTED COMPANIES 2013 UK BUILDING REGULATIONS REVISION 2011 INSPECTION OF A/C SYSTEMS >12kW 2011 RENEWABLE HEAT INCENTIVE SCHEME AVAILABLE FOR INDUSTRY 2011 GREEN DEAL LOANS AVAILABLE FOR ENERGY REDUCTION TO EXISTING 2010 UK BUILDING REGULATIONS REVISION 2010 MANDATORY CARBON REDUCTION COMMITMENT (CIRCEES) 2009 DEER LOW CARBON INDUSTRIAL STRATEGY 2009 INSPECTION OF A/C SYSTEMS >250kW 2008 EPCs/DECs REQUIRE FOR ALL BUILDINGS 2008 CLIMATE CHANGE ACT - THE COMMITTEE ON CLIMATE CHANGE 2007 UKGBC REPORT FOR NON-DOMESTIC BUILDINGS 2007 CODE FOR SUSTAINABLE HOMES 2006 UK BUILDING REGULATIONS PARTS F + L BASED ON CARBON TAKE 2005 ORD STERN'S REVIEW - ECONOMIC CASE FOR ACTION	2020
2010	2015 RGGI CAP TIGHTENS 2.5%/PA TILL 2020 (CT, DE, ME, MD, MA, NH, NJ, NY, RI, VT) 2014 RGGI CAP TIGHTENED TO 91M SHORT TONS (CT, DE, ME, MD, MA, NH, NJ, NY, RI, VT) 2012 RGGI CAP TIGHTENED (CT, DE, ME, MD, MA, NH, NJ, NY, RI, VT) 2009 RGGI CAP TIGHTENED (CT, DE, ME, MD, MA, NH, NJ, NY, RI, VT) 2009 AMERICAN CLEAN AIR AND SECURITY BILL (ACAS) 2007 ENERGY INDEPENDENCE AND SECURITY ACT (EISA) 2005 ENERGY POLICY ACT 2005 RGGI CO2 CAP (CT, DE, ME, MD, MA, NH, NJ, NY, RI, VT)	ENERGY EFFICIENCY DIRECTIVE (2012/27/EU) EU TARGET FOR RENEWABLES 22%		2010
2000	2005 GB GLENEAGLES - REVERSE GREENHOUSE GAS EMISSIONS 2002 JOHANNESBURG EARTH SUMMIT 1999 CEMENT INDUSTRY WORLD SUSTAINABILITY INITIATIVE (CSI) 1997 KYOTO CONFERENCE ON GLOBAL WARMING - MANDATORY EMISSIONS LIMITATIONS	EU-ETS ENERGY TRADING SCHEME DIRECTIVE (2004/101/EC) ENERGY PERFORMANCE OF BUILDING DIRECTIVE (2002/91/EC) EU RENEWABLES DIRECTIVE (2001/77/EC)	2000-2002 UK BUILDING REGULATIONS 2000-2002 - PRESCRIPTIVE ENERGY STANDARDS	2000
1990	1992 RIO EARTH SUMMIT - AGENDA 21 1990 CARBON EMISSIONS CALCULATION BASELINE FOR "RAGE IMPROVEMENTS" 1987 MONTREAL PROTOCOL ON OZONE LAYER DEPLETION 1987 BRUNDTLAND COMMISSION "OUR COMMON FUTURE"	1993 USGBC FOUNDED)	1990 BREEAM AVAILABLE FOR ALL OFFICES + INDUSTRIAL BRE LAUNCHES BREEAM FOR NEW OFFICES	1990
1980	1983 HELSINKI PROTOCOL ON AIR QUALITY 1980 WORLD CONSERVATION STRATEGY 1979 GENEVA CONVENTION 1979 BERNE CONVENTION	1996 EUROPEAN ENVIRONMENT AGENCY (EA) 1993 MAASTRICHT TREATY ON EUROPEAN UNION 1990 EC GREEN PAPER ON URBAN ENVIRONMENT		1980
1970	1972 "LIMITS TO GROWTH" REPORT			1970

4 Regulation

4.1 Introduction

Approximately 60% of the energy consumed by dosage form (secondary) manufacturing and biotechnology operations is by environmental control systems. The principal consumers of the energy include Heating, Ventilation, and Air Conditioning (HVAC) systems, fans, and their associated chilling and cooling systems. Such systems contribute significantly to both the manufacturing cost and the carbon footprint of the manufacturing operation. In the case of API (primary) manufacture a greater proportion of the energy is consumed by the process.

A significant amount of energy can be consumed by clean and facility utilities that drive or support process and process equipment.

Sustainability issues associated with water consumption and effluent should also be considered. For example, in some regions of the world, water shortage is leading to risk-based thinking about recycling of rinse water.

4.1.1 *The Agency Response: FDA, EMA, and Other Agencies*

The regulatory bodies' response to sustainability is to encourage innovation through the adoption of risk based strategies and stated acceptance of closed and continuous processing principles.

This frees up the capacity for the companies to consider options for reductions in clean backgrounds and more efficient methodologies from such as real-time particulate testing allowing reductions in air volumes and the potential for air recycling to capacity to adjust grade steps allowing complementary reductions in air movement/volumes while still retaining necessary safety controls.

4.2 Energy Management Systems

As an initial step to make efficiency improvements in both new and existing facilities, it is recommended that commitment to energy management be obtained at the appropriate management level. Effective organizational structures should also be established.

Adoption of an Energy Management System (EMS) compliant with ISO 50001:2011 [17] should be considered. Organizations may either follow and adopt the principles of the standard, or implement it and seek formal accreditation. This standard is analogous to ISO 9001:2008 [53] and ISO 14001:2015 [16].

ISO 50001:2011 [17] requires that an organization establish a clear framework and strategy for understanding where energy is consumed, and plan and implement an energy use reduction and monitoring program. Using such a framework, measures can be implemented to reduce energy costs, the carbon footprint, or both.

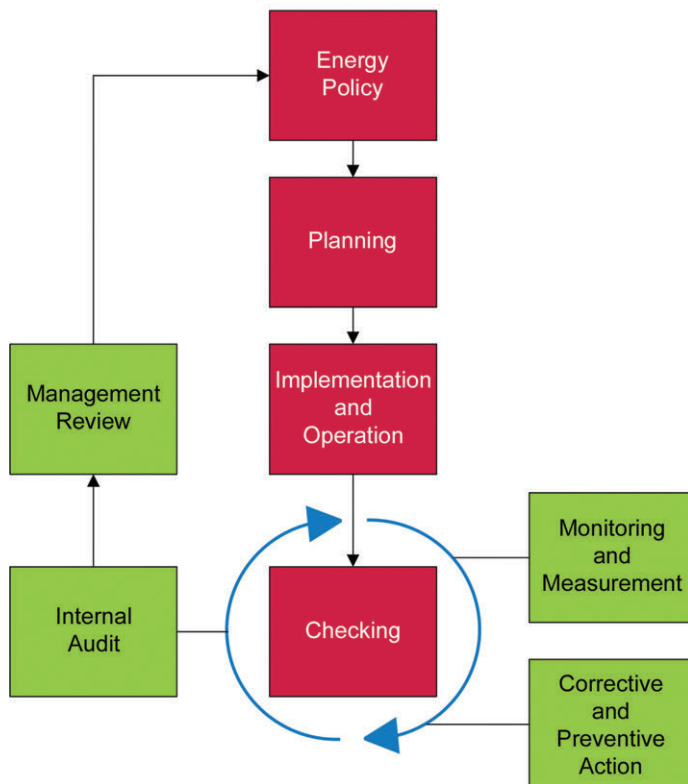
Benefits of an ISO 50001:2011 [17] include:

- A framework for integrating energy efficiency into management practices
- Making better use of existing energy consuming assets
- Benchmarking, measuring, documenting, and reporting energy intensity improvements and their projected effect on reductions in greenhouse gas emissions
- Transparency and communication on the management of energy resources
- Commitment to financial and human resources to deliver energy reduction programs



- Energy management best practices and good energy management behaviors
- Evaluating and prioritizing the implementation of new energy efficient technologies
- A framework for promoting energy efficiency throughout the supply chain
- A basis for continual improvement

Figure 4.1: Compliant ISO 50001:2011



The flow diagram in Figure 4.1 illustrates the essential stages and key principles underlying a compliant ISO 50001:2011 [17]:

- **Plan:** Establish the sustainability objectives and sustainability targets required to deliver results in accordance with the policy.
- **Do:** Implement the actions required to achieve the sustainability objectives.
- **Check:** Monitor and measure against the policy, objectives and targets set.
- **Act:** Take actions to improve sustainable actions, including, e.g., reductions in use of solvents, improvements in energy performance, etc.

The section in ISO 50001:2011 [17] on “Planning and EMS” sets out the following principles in the normative section of the standard:

- Compile good quality information on past and present energy consumption and energy factors based on measurement and other data.

- Identify areas of significant energy consumption, especially for significant changes in energy use during recent periods of time.
- Estimate expected energy consumption during future periods of time.
- Identify all persons working for and on behalf of the organization whose actions may lead to significant changes in energy consumption.
- Identify and prioritize opportunities to improve energy efficiency.
- Maintain a register of opportunities for saving energy.
- Document reviews of energy consumption.

The guidance on implementation of an energy management program could refer to the corporate approach or be focused on a specific energy saving project. In order to implement an EMS, an organization should:

- Provide adequate resources and authorities to implement the program
- Designate a management representative for the EMS
- Provide awareness and competence training
- Communicate internally
- Decide whether to communicate externally
- Have an operable document control system in place
- Have effective operational controls in place (e.g., to identify deviations and remedy them)
- Have effective monitoring in place
- Compare to industry benchmarks, where possible
- Evaluate compliance
- Undertake routine management reviews and report compliance/deviations and actions taken

Overall, ISO 50001:2011 [17] gives organizations a structure to help them commit to managing throughout their entire structure. It makes responsibilities and accountabilities clear and commits senior management to engage in energy management. It calls for organizations to document the policy that is going to be used and drives energy planning to consider historical use, process use and identifying objectives and targets for future use.

Clear methods of identifying non-conformity and details of corrective action to be taken should also be developed.

As well as reductions in energy use, ISO 50001:2011 [17] also looks at the procurement of energy by the organization.

If properly implemented, ISO 50001:2011 [17] will increase the knowledge of the energy use and put in place a method to reduce it within an organization. This, combined with clear roles and responsibilities it establishes and the commitment it gets from senior management, means that it is very likely indeed to result in reduced energy use.

4.2.1 Operating without Instituting ISO

ISO 50001:2011 [17] is considered a good way to identify and drive energy management in facilities, but whether the process is implemented or not, the desired changes are:

- Behavioral:
 - Occupants, operators, and building managers are key to ensuring building energy use is understood, controlled, and improved
 - Occupants, operators, and building managers should understand the drive to improve energy use.
 - The desire to improve energy use should be led from a senior level and demonstrated as a priority by the business
 - Occupants, operators, and building managers should:
 - » Understand existing energy use and know how to improve and manage energy consumption
 - » Know when the changes they are making are improving consumption and when improvements are not being achieved. Adequate metering and monitoring needs to be established.
- Engineering:
 - Reducing energy use by engineering changes should be justified and verified. Without an awareness of energy use, the justification can be difficult and investment can be harder to secure.
 - The metering of energy use is, therefore, helpful to identify opportunities and is vital to recognizing the savings achieved.
 - Engineering changes should be based upon realistic objectives and solutions. They should take into account the use of the space and the regulatory, user, and safety requirements.
 - Change control should be linked to quality assurance and operating maintenance, etc.

4.3 Achieving Energy Reduction

Achieving the delivery of new energy efficient facilities and equipment, or the improvement of the performance of existing facilities requires an appropriate management structure, technical competence, and documented best practice to operate together.

The management structure can be applied through either a formal or an informal implementation of the principles of ISO 50001:2011 [17]. It should provide an environment that encourages the delivery of energy conservation programs. The management structure should be integrated with appropriate technical competence and documented best practice.

Good Engineering Practice (GEP) includes competence in energy sensitive design and specification. Part of a professional engineer's remit includes the application of GEP. Guidance that identifies key areas to be considered, or principles that should be adopted, when trying to achieve energy efficient solutions can be helpful to professional engineers. The *ISPE Good Practice Guide: Heating, Ventilation, and Air Conditioning (HVAC)* [54] considers GEP related to the engineering of environmental control systems. The guide illustrates typical HVAC system configurations,

and identifies areas where energy saving might be achieved through low energy design and silent-hour system setback. Opportunities for energy reduction in HVAC and environmental control systems lie in:

- Low-resistance designs
- Optimized cleanliness levels
- Air volumes
- Temperature and humidity levels
- Setback conditions during unoccupied periods

Utility infrastructure – including solutions such as combined heat and power (CHP) or trigeneration (trigen) systems and use of phase change cooling storage – may be considered as opportunities for achieving energy cost reductions, depending upon the local supply energy mix and incentives available.

Improving specific unit process operations should also be considered. There is a potential for process optimization using PAT techniques to bring significant advantages in process cycle reduction and associated energy consumption reduction. For example, in lyophilizer applications the measurement of real product quality attributes can give rise to cycle time reductions of 20% to 30%, with the associated energy reduction. Sustainability and quality aspects should be considered holistically, to seek maximum benefits from efforts to reduce energy.

There is also potential for significant savings in water usage and generation of wastewater through improved equipment and piping design, and cleaning cycle optimization.

Published Standards

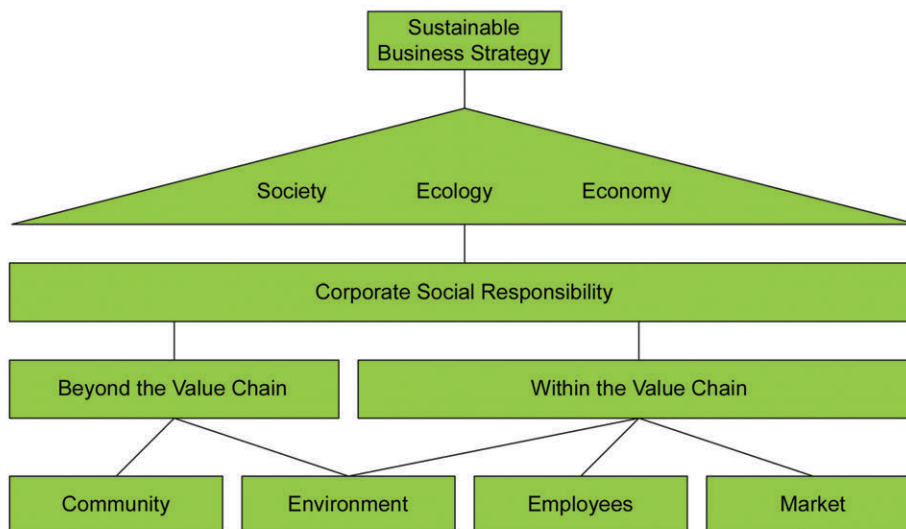
Other published standards are related specifically to cleanroom applications and include:

- VDI 2083 Sheet 4.2: Cleanroom Technology – Energy Efficiency [55]
 - Published in April 2011
 - It provides specific cleanroom-related energy saving guidance.
 - It contains some interpretation of German national requirements and engineering practices
 - It contains suggestions that affect both the configuration of handling systems and their operation
- BS 8568:2013: Cleanroom Energy. Code of Practice for Improving Energy Efficiency in Cleanrooms and Clean Air Devices [56]:
 - Published specifically to address cleanroom and clean zone technology and to identify areas where energy saving might be achieved in both existing and new facilities. The standard is written as a code of practice in support of ISO 50001:2011 [17].
 - Contains a checklist of energy saving opportunities. This checklist also has a column that identifies areas of risk associated with energy saving measures. For example, if a clean room is provided with air volume setback during silent hours, then the HVAC system is inherently more complex. This increased complexity gives rise to a greater likelihood of component or system failure. This risk should clearly be identified during a current Good Manufacturing Practice (cGMP) related design review of proposals to modify an existing system or of a new facility design.

5 Sustainability Policy Development

This chapter outlines the reasons for and components of corporate sustainability policies for the life sciences industry. It is intended as a guide for developing and delivering a policy that fits, challenges, and improves an organization. Sustainability may be considered a key component of a business strategy, as both are associated with long-term success. In his 2009 book *The Global Emerging Market* [57], Economist Vladimir Kvint defined strategy as “a system of finding, formulating, and developing a doctrine that will ensure long-term success if followed faithfully.”

Figure 5.1: Sustainable Business Strategy



5.1 Reasons to Create a Sustainability Policy

In addition to protecting the environment, sustainability offers business benefits ranging from cost savings to public approval. The authors of “UN Global Compact – Accenture CEO Study on Sustainability 2013” suggest that sustainable policy can lead to value creation, citing such opportunities as performance measurement and innovation [58].

5.1.1 Direct Benefits

Employee Health and Productivity

Sustainable facilities are associated with increased employee health and productivity. In the LEED Platinum-certified Genzyme Center, 72% of surveyed users reported feeling more alert and productive than in their previous workplace [59].

Operational Cost Savings

Sustainable facilities and transportation are associated with energy savings. In 2012, the global medical technology firm Becton Dickinson and Company attributed \$482,000 in savings to its 12 LEED-certified facilities [60]. Profits may be increased due to decreased product manufacture and distributions costs.

Tax Credits and Local Incentives

Tax credits and other incentives may be available for sustainable measures such as energy conserving building design, brownfield or blight redevelopment, and sustainable business practices. National and local jurisdictions should be checked for applicable incentives at each facility.

5.1.2 **Indirect Benefits**

Indirect benefits include:

- Consumer appeal
- Investor appeal
- Manage risks and create value
- Enforced environmental policies (see Section 3)

5.1.3 **Environmental Stewardship**

Organizations exceeding governmental regulations may choose to do so in order to sustain the environment in which they do business. The pharmaceutical and medical device industries accounted for almost half the carbon footprint of England's National Health Service in 2010 [61]. In 2007, the health care sector accounted for 8% of total US greenhouse gas emissions and 7% of total CO₂ emissions [62].

5.2 **Setting Goals**

5.2.1 **Corporate Sustainability Policy**

Organizations should consider corporate values, all applicable regulations, and feasibility when considering which elements to include in a corporate sustainability policy. A list of components to consider when drafting or revising a corporate sustainability policy is provided in Appendix 2.

5.2.2 **Determining Goals: Methods and Thresholds**

Research Environmental Regulations

Organizations may choose to comply only with environmental regulations for each relevant jurisdiction or to exceed regulations. Relevant environmental regulations should be researched before developing a sustainability policy. Synergies between reporting formats and potential internal reporting policies should be identified. Any further investment required to achieve third party certifications, such as LEED, should be determined.

Corporations may find that environmental certification is feasible with little or no further costs beyond building code and other legislative requirements (e.g., national standards or codes of practice, and common manufacturing practices). For additional information on synergies between pharmaceutical practices and environmental building assessment, see Chapter 6.

Monitoring Competitors

Where corporations are interested in meeting or exceeding competitors, the actions of similar corporations to communicate their sustainability policies to the public should be monitored.

Creating or Adopting a Management and Reporting System

Many existing standards can be adopted to measure environmentally sustainable facilities, such as LEED, BREEAM, and American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE) guidelines [63]. Other standards can be adopted for ongoing management and quantification of sustainable operations, including:

- ISO 14006:2011 [64]

- European Union's Eco-Management and Audit Scheme (EMAS) [65]
- Energy Star® PortfolioManager® [66]
- Global Reporting Initiative (GRI) [67]
- United Nations Global Compact (UNGC) [58]

Many life sciences organizations have committed to these standards, either voluntarily or because of regulatory requirements.

Organization-specific forms can be created instead of, or in addition to, existing management formats. The desired type of management, frequency of reporting and review, and labor costs that are feasible to implement the system should be considered.

Seeking External Assistance

Organizations are available to assist in devising and implementing a sustainability policy:

- The US based Rocky Mountain Institute's (RMI) online "Knowledge Center" [68] is a good resource for industry and region specific data on current and upcoming energy technologies and reduction strategies
- UK based Carbon Trust [69] is a not for dividend consulting company aimed at helping governments and organizations reduce carbon emissions and save energy costs
- Independent auditors, such as ISO 14001 EMS consultants
- Commercial sustainability focused consultancies [70]

5.3 Promoting Initiatives

5.3.1 Promoting Initiatives Internally

Obtaining employee buy-in and compliance can be complex in a multinational organization. The following methods may be used:

- Mandatory compliance reports
- Employee incentives for sustainable choices, such as public transit subsidies and priority parking for carpools, or working from home
- Sustainability awards to employees or individual sites for achieving or exceeding goals

5.3.2 Promoting Initiatives Externally

Options for publishing goals and performance data should be considered for data and outputs that are not regulated externally. Organizations may find it appealing to show performance data compared to the organization's previous performance, which can demonstrate incremental reductions in resources and emissions. Some vociferous critics, however, often deem this practice as misleading and call for industry transformations that are easy to verify [71]. The term "greenwashing" may be applied to environmental claims that are not backed up by real data.

Global life sciences organizations, by either legislation or choice, often show past years' sustainability achievements and future goals in their annual Corporate Social Responsibility (CSR) report, or within a "responsibility" section of the organization's website.

5.4 Management

Developing Company Sustainability Reporting Standards

Information which needs to be reported in order to manage the corporate sustainability policy should be identified. The required frequency of reports and associated responsibilities, e.g., submitted by whom and to whom, should be determined. Formats normally used for other requirements, such as regulatory compliance and existing corporate initiatives, should be identified. It may be possible to identify reporting formats that satisfy several requirements at once.

Existing management formats and software may include components for assessing sustainable design and environmental reporting, e.g.:

- Operations management software such as SAP and ERA can track complex data related to resources, energy demand, and equipment maintenance
- Management formats such as EMAS and ISO 14001
- Standards for facility design, such as ASHRAE, CIBSE and similar national environmental engineering society standards or design initiatives such as LEED and BREEAM (see Chapter 4)
- Standard company forms, e.g.:
 - Facility sustainability scorecard
 - Facility energy use records
 - Total energy use by fuel type
 - Energy use by building system
 - Facility greenhouse gas emissions records
 - Transportation fuel use and emissions records
 - Life cycle emissions of purchased products
 - Total company emissions (see ISO 14064-1:2006 [72] for guidelines on total company emissions assessment)

Projecting First Cost for Sustainability Policy Implementation

First costs may vary significantly by organization, depending on:

- Personnel costs for creation and review of sustainability policy
- Sustainable design fees and construction costs
- Equipment replacement and upgrade costs
- Building certification (e.g., LEED) fees

Percentage of Ongoing Cost to Put into Sustainability Staff, Consultants, and Resources

A comparison against other organizations may be useful.

Organizations should consider whether the personnel requirements of a sustainability policy are better fulfilled by consultants, existing staff, or by hiring new, dedicated personnel.

Ongoing costs and returns of a sustainability policy will vary, depending on several components, e.g.:

- Costs of:
 - Environmental management software licensing
 - Green power and/or carbon offsets
 - Green cleaning and waste removal companies
 - » Costs should be verified with service providers to determine if there is added cost for green cleaning and waste management; it may be included in standard procedures.
 - Sustainability verification and/or audits
 - Personnel for policy implementation and performance review
 - Public relations personnel for publicizing sustainability goals and achievements
- Savings in:
 - Utility costs compared with those for existing or conventionally designed facilities
 - Utility costs over conventional manufacturing and laboratory equipment
 - Rebates and incentives for sustainable design and operations
 - » National and local incentives should be verified.

5.5 Predicting and Measuring Performance

Financial Success of Sustainable Measures

Organizations may associate environmental sustainability with philanthropy, assuming it delivers only intangible outcomes; however this assumption can be dispelled by tracking data or measuring progress. ROI is typically calculated as:

$$\text{Net income before taxes} \div \text{Total amount invested}$$

This can be modified to measure sustainable investments. For example, to measure the utility savings in an existing or proposed energy efficient building system over a given amount of time, ROI could be calculated as:

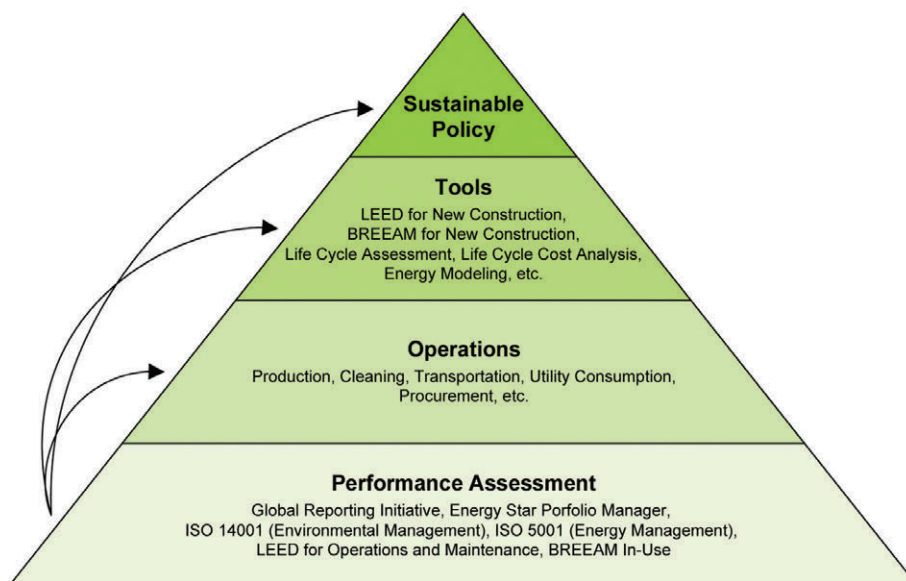
$$\frac{(\text{Utility cost of traditional system} - \text{Utility cost of sustainable system})}{\div (\text{Initial cost of sustainable system} - \text{Initial cost of traditional system})}$$

Life cycle costs, such as the utility costs, can be predicted before implementation by using software such as whole building energy modeling, or whole building life cycle assessment. Data management after implementation can be used to compare actual results to predictions.

Environmental Success of Sustainable Measures

- Comparison of results to goals:
 - Did the organization meet sustainability goals in the reporting period (per week, month, or year)?
- Comparison of different facilities within the organization:
 - Which facilities did best? Worst?
 - How does climate in specific locations affect energy use?
 - Does the fuel source (gasoline, coal, petroleum coke, etc.,) affect emissions in specific locations?
- Comparison (or benchmarking) of similar facilities within other organizations:
 - This is particularly useful where other organizations have facilities in the same region, with similar climate and greenhouse gas emissions per unit of energy.
- Combining all results for total corporate performance data:
 - See guidance in ISO 14064-1:2006 [72]
- Environmental performance of sustainable measures can be predicted using software for whole building energy modeling and whole building life cycle assessment

Figure 5.2: Performance Assessment as a Means of Policy Feedback



6 Sustainability Assessment for Buildings and Products

6.1 Introduction

There are many rating systems to assess the sustainability of buildings and products. Systems such as the US-based LEED and UK-based BREEAM are intended to rate the design, construction, and operation of buildings, resulting in an overall score that may attain certification at various levels. Similar rating systems are available to assess aspects of manufactured products such as material sourcing, embedded energy, and embedded carbon. Sustainable product assessment can lead to certification through the third party assessment agency, earning a label that may be added to product packaging or literature. Although sustainable product assessment has seen limited popularity in the life science industry at the time of this publication, sustainable building assessment is a major component of many corporate policies in the life science industry (see Appendix 3).

6.2 Benefits of Building Assessment

Public Relations Benefits

- A 2011 study [73] shows that more than twice as many consumers are convinced by third party eco-labeling than by claims of being “environmentally friendly.”
- Building assessment systems offer recognizable and third-party verified ratings, in a market where consumers are inundated with claims of sustainability based performance characteristics that are difficult to prove.

Reduction of Energy Costs and Emissions

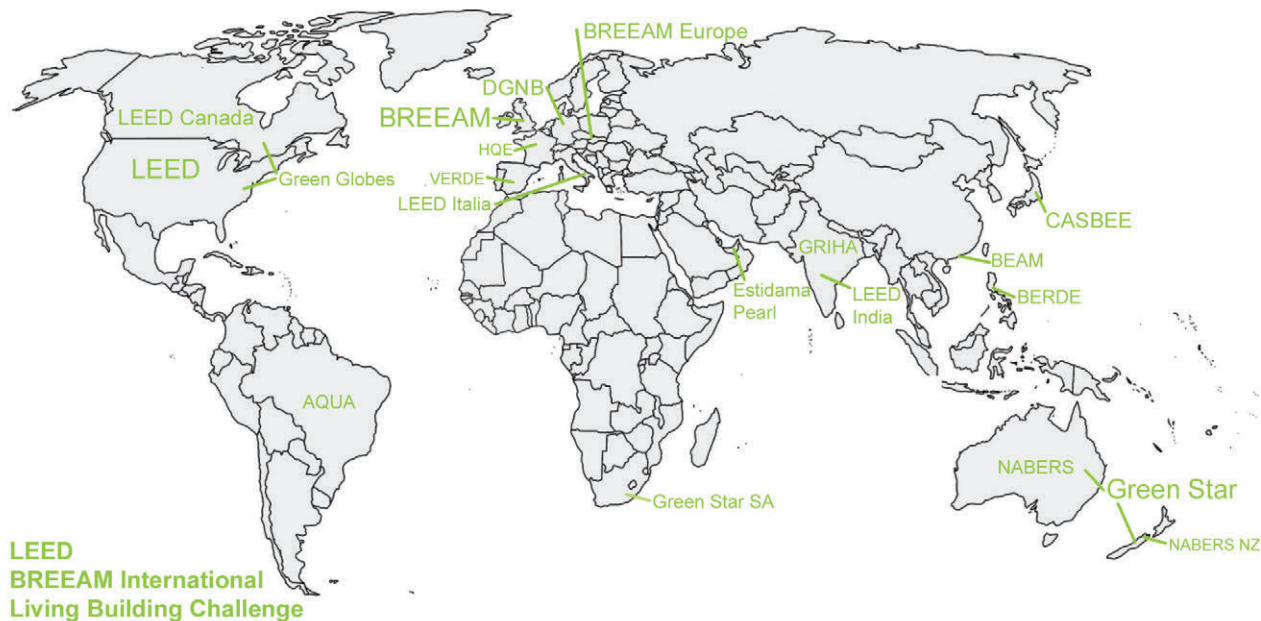
- LEED-certified buildings use on average 25% to 30% less energy than conventional buildings and cost, on average, only 2% more to build [74]
- Increased property value
- A 2010 study [75] found that LEED certification increased commercial real estate values over conventional buildings in some cities

Financial Incentives

- Tax credits and other incentives may be available for participation in building-assessment schemes. National and local jurisdictions should be checked for applicable incentives for each facility location.

6.3 Current Building Assessment Systems

Figure 6.1 Global Rating System Distribution



Note: Some rating systems, such as LEED, BREEAM International, and Living Building Challenge are available internationally. See Appendix 3 for links to most of the world's building based environmental rating systems.

Building rating systems assess the design, construction, operation, and maintenance of buildings. The systems score buildings based on sustainable attributes, resulting in ratings using various terms ranging from "Class C" or "Not Certified" to "Class S" or "Platinum." Most systems rate buildings using a system of points or credits, from which projects may choose the most advantageous sustainability initiatives for the project. Credits are typically divided into categories such as:

- Water efficiency
- Site design
- Energy efficiency

These types of rating systems typically have a scorecard with different point values assigned to various measures of sustainable design.

Alternatively, holistic scoring systems, such as the Japanese CASBEE, may be more rigorous by evaluating all projects by the same criteria. National and local availability should be checked to identify available rating systems. Global examples of rating systems include:

- BREEAM:

A UK-based system with National Scheme Operators in several European countries, as well as a BREEAM International system available since 2013. Buildings can attain certification by scoring points to meet thresholds from "Pass" to "Outstanding."

- LEED:

Originally developed by the US Green Building Council, LEED's most recent incarnation (LEED v4) has been designed for international implementation. The point-based system awards certification for projects meeting thresholds ranging from "Certified" to "Platinum."

- Green Globes:

Based on BREEAM, this Canadian system is offered in Canada and the US. The point-based system awards projects one to four "Globes" to indicate certification levels.

- Green Star:

This system has versions available in both Australia and South Africa. The point-based scoring awards projects a minimum of one star, up to a rating of 6 stars.

- Deutsche Gesellschaft für Nachhaltiges Bauen (DGNB) [76]:

This German rating system is also available in several European, Asian, and South American countries. Like most rating systems, DGNB scores buildings and urban developments in categories such as environmental, sociocultural, and technical quality. It differs from other point-based systems in that no categories can be omitted from the project scorecard, and the scoring has a unique focus on LCA and life cycle cost assessment (LCCA). See Chapter 12 for more on LCA and LCCA.

- Comprehensive Assessment System for Built Environment Efficiency (CASBEE) [77]:

This Japanese tool is not point based, but rather spreadsheet based. It produces a holistic score, which is the ratio of "Quality," or the building's environmental and functional benefits, over "Load," or its environmental demands. This ratio "Q/L" results in a sustainability rating ranging from "Class C" (Poor) to "Class S" (Excellent).

6.4 Facility Assessment Systems versus Custom Facility Performance Goals

Organizations should decide whether to align their sustainable measures with what is feasible for the organization, or to modify their sustainable measures to meet a green building rating system.

Advantages of life sciences facilities for green ratings:

- Many common design and operations features of life sciences facility buildings already meet many criteria for rating systems such as LEED and BREEAM. Life sciences facilities can be at an additional advantage when point-based systems allow specific environmental aspects of facilities to remain unchecked, such as process utility loads and building materials not included in credit calculations. Table 6.1 highlights the advantages, as well as a few difficulties, in achieving environmental building rating for pharmaceutical facilities.

Table 6.1: Environmental Rating Systems for Pharmaceutical Facilities

Pharmaceutical Practice	Rating System Feasibility	Comments
Water		
Water monitoring	Advantage	BREEAM currently rewards facilities for this practice; LEED v4 does the same.
Energy		
Systems commissioning	Advantage	Both LEED and BREEAM reward projects for sophisticated testing and oversight of the building's systems.
Exclusion of process equipment from regulated loads	Advantage	Energy models are not penalized for heavy process loads; however, this is a missed opportunity to innovate.
Energy monitoring	Advantage	The common pharmaceutical practice of monitoring energy use or installing sub-meters is rewarded as a sustainable practice.
Materials		
Low use of wood	Advantage	Both LEED and BREEAM reward projects using sustainably harvested wood as a percentage of total project wood. Life sciences projects with little wood have a smaller threshold to meet. This scoring advantage may not incentivize the most sustainable material choices though, because alternatives to wood often have higher embedded carbon.
Indoor Health		
High airflow rates	Advantage	Although this poses a difficulty for energy credits, the amount of clean air being delivered to spaces can score points for air quality.
High-performance air filtration	Advantage	Air-filtration standards for manufacturing spaces usually exceed those required by rating systems.
High-performance paints and coatings	Difficulty	GMP facilities usually require high-performance coatings (conductive, non-corrosive primers, etc.), which usually exceed allowable Volatile Organic Compound (VOC) content. A materials procurement policy that limits VOCs should be considered.
Constant lighting at process areas	Difficulty	Rating systems prefer occupancy sensors and user-controlled lighting.
Few exterior windows	Difficulty	Fewer opportunities to provide natural light and ventilation.

Downfalls of rating systems for life sciences facilities:

- Designing to a rating system may lead organizations away from some of the most project-specific sustainable measures. Although several subsystems based on building type are available, life sciences facilities are difficult to stereotype, frequently being some combination of laboratory, factory, warehouse, or office. Green building rating systems can miss opportunities to encourage sustainable operational policies such as cleaning, product packaging, and waste management. These opportunities to encourage sustainable operational policies should be considered for life sciences facilities where such ongoing operations can be critical.

Rating systems for existing building operations rather than facilities in design:

- This may be advantageous for organizations with an existing building stock where a new sustainable design is not possible, or for sustainable policies that focus on innovative operations rather than design. Schemes such as Green Star Performance, BREEAM In-Use, and LEED for Existing Buildings, can address these criteria.

International use of a single rating system:

- For corporate benchmarking purposes, a global organization may wish to use a single internationally recognized assessment system. LEED v4 and BREEAM International offer schemes for international implementation. In addition to international implementation, the scheme's recognition in countries with consumers and stakeholders should be considered.

6.5 Product Rating Systems

There are rating systems available to evaluate the sustainable features of manufactured products. Manufacturers may earn a sustainability label for products meeting specific criteria. There are several options for labeling a product with information about its environmental attributes. Labeling options range from general to specific and from self-declared to third party verified. The International Organization for Standardization (ISO) maintains standards for various types of product environmental labeling:

- ISO 14024:1999 Environmental Labels and Declarations – Type I Environmental Labeling – Principles and Procedures [78]:
 - This section specifies the procedures and principles that third party certifiers or multi-attribute eco-labelers, must follow. Among the most important of these relate to use of sound scientific methods and accepted test procedures, openness and transparency in the setting of standards, and avoidance of financial conflict of interest.
 - A directory of third party eco-labeling companies is maintained by the non-profit Global Ecolabeling Network, or GEN [79].
- ISO 14021:1999 Environmental Labels and Declarations – Self-Declared Environmental Claims (Type II Environmental Labeling) [80]:
 - These are intended for communication from the product manufacturer to consumers. They do not necessarily address all aspects of a product's life cycle, but ISO provides general guidelines to convey the following product attributes, as applicable:
 - » Reduced resource use
 - » Recovered energy
 - » Waste reduction
 - » Reduced energy consumption
 - » Reduced water consumption
 - » Extended life product
 - » Reusable and refillable

- » Designed for disassembly
 - » Compostable
 - » Degradable
 - » Recyclable
 - » Recycled content
- ISO 14025:2006 Environmental Labels and Declarations – Type III Environmental Declarations – Principles and Procedures [81]:
 - Type III Environmental Product Declarations (EPDs) are considered the most stringent and transparent type of product label within the ISO 14000 series, allowing for “apples-to-apples” product comparisons. It is an internationally recognized labeling standard that documents the ways in which a product’s life cycle affects the environment.
 - Type III EPDs as described in ISO 14025:2006 [81] were originally intended for use in business-to-business communication, but they are gaining increasing recognition with consumers. The first medicinal EPD was verified in 2011 for a veterinary vaccine manufactured by Pfizer [82].
 - The steps to obtaining an EPD for a specific product are:
 1. Find an appropriate Product Category Rule (PCR):
 - » The first step in creating an EPD is to find or create a PCR that is applicable to a particular product type. The rules set forth in a PCR allow products of similar types to be evaluated under the same criteria.
 - » If a PCR does not yet exist for the product seeking an EPD, a new PCR will need to be issued by a third party program operator.
 - » A directory of existing and proposed PCRs can be found with the non-profit Global Environmental Declarations Network [83], and EPD International, [84] which maintains a website maintained by the Swedish Environmental Management Council, the body that oversees EPDs.
 2. Conduct and verify the product LCA:
 - » Once an ISO 14040:2006 [85] LCA is conducted on a particular product, it must be verified by an independent party to ensure it meets the requirements defined in the product category rules.
 3. Compile the EPD:
 - » The EPD presents the results of the LCA along with additional information about the product’s performance and other sustainability attributes.
 4. Verify the EPD:
 - » An independent third party conducts a review and verification of the EPD results.
 5. Register the EPD:
 - » The program operator adds the EPD to its list of registered EPDs.

7 Future Directions and Opportunities

7.1 Introduction

It is highly likely that general adoption of sustainable systems will become the norm worldwide and encompassed in most countries' building, energy use, and health and safety legislation, as it is already within the EU and Australia, if not driven by ethical concerns.

Until the first adopters prove that inclusion of sustainability based formats provide a significant payback, sustainability is unlikely to be adopted by the rest unless forced or through conscience.

Some areas where improvement and/or adoption of sustainable systems are likely, other than through the mechanical engineering returns apparent from changes in the clean environmental controls and throughput volumes, include:

- Integration
- Changing structures
- Developing World opportunities
- Size reduction
- Cost validity
- New materials, manufacturing processes, and transportation methods

Integration

- Facilities and processes:
 - Changes in facility design and concept reflecting the reductions in manufacturing equipment size available through closed, continuous, and modular system formats, leading to a baseline reduction in energy usage.
 - Concerns about drug shortages, available throughput using batch based systems, inconsistency of quality leading to waste resultant from poor batches, significant throughput times, and the amount of intermediate stock hold have driven a number of programs considering and implementing prototype continuous processes.
 - A reluctance to change. These processes challenge the norm in terms of the need for some currently powerful departments and staff. The fear of regulatory failure has tended to place these exercises on the shelf. The stage of development of PAT ensuring reliable in-process characterization and consistency has not been entirely closed out. Current developments have begun to close this concern, with improving technology.
- Acceptance of multiple and mixed use product facilities (e.g., biopharmaceutical existing in the same facility as oral solid dose manufacturing) resulting in better use of the energy available.
- Design of equipment to better balance heat output and usage. Using phase change, heat transfer, and exchange methodologies, i.e., acceptance that heat or cooling output will not be dealt with by the building and HVAC systems and that process plant is designed to be energy neutral.
- Some reactions may provide sufficient output to retain a facility at zero external energy usage, dependent on climate zone.

- Use of energy from site-sourced renewable resources, providing a return to the community at large.
- Significant advances in green chemistry reducing the need for solvents
- Significant increase in the integration of renewables systems into facility design, e.g., Building Integrated Photovoltaics (BIPV)
- Controls and monitoring:
 - Facility Control Systems (FCS) that deal with the integration, monitoring, and control of the total facility energy and operational management, driving significantly greater integration between the building and the process in energy usage
 - Integrated data systems providing the capacity to better control the supply chain using sustainability based algorithms

Changing Structures

Some question the use of energy or carbon trading as a solution to the amelioration of release of greenhouse gases or as a balance against carbon issues. The concern is that it will become impossible to monitor the off-sets traded or the trees planted. Some consider that such trading is avoiding the issue of seeking a practical local response to a physical problem.

Developing World Opportunities

Projects in developing countries provide an opportunity for the fulfillment of a sustainable objective through the transportation of only necessary resources for long distances. This has a direct impact on the approach to End to End (E2E) supply chain operation and challenges the growth method and investment in the Developing World. The development of sustainable opportunities in this area may be beneficial to both Developed and Developing World operations.

Size Reduction

Compact processes:

- Significant improvements in process yield available through improvements in pharmaceutical and biologics science and manufacturing methodologies allow reductions in the size and number of manufacturing facilities needed, with consequential increased flexibility and sustainability gains.
- The use of smaller systems monitored by PAT developments and adoption of continuous processing will additionally mean smaller facilities, smaller areas of controlled containment and potential for further significant sustainability gain.
- The opportunity lies in the provision of significantly smaller, more responsive, agile, flexible, and, by definition, sustainable plants, providing consistent quality throughput. The size reduction available also allows the consideration of highly complex but reliable manufacturing pods and modules with the capacity to be placed in:
 - Localized world locations to reduce time to patient with the aim of satisfying epidemic pull demand
 - Tandem or multiple mode to ensure multi-product streamed production from API to secondary with quality surety
 - Flexible facilities allowing interchange between product dosage forms and formats, development, or production modes dependent on need