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RESEARCH ARTICLE

CHALLENGES OF DEVELOPING DECISION-SUPPORT TOOLS BASED ON LIFE CYCLE ASSESSMENT (LCA) FOR THE BIOPHARMACEUTICAL INDUSTRY

S. RAMASAMY*, N. TITCHENER-HOOKER* AND P. LETTIERI**

**The Advanced Centre for Biochemical Engineering, Department of Biochemical Engineering, University College London, Torrington Place, London WC1E 7JE, UK*

***Department of Chemical Engineering, University College London, Gower Street, London WC1E 7JE, UK*

SUMMARY: The biopharmaceutical industry has been slow in carrying out LCA analyses. However, as the industry matures, the level of scrutiny placed on this industry by international governments will increase and hence, there is an urgent need for the industry to implement decision-support tools for the decision-making processes. Decision-support tools based on life cycle assessment (LCA) can be potentially used for application in the biopharmaceutical industry as an aid to decision making. This paper sets out the challenges associated with developing such decision-support LCA tools. This paper highlights that in order for the industry to overcome these challenges and successfully develop decision-support LCA tools, they require a broader understanding of the biopharmaceutical manufacturing processes and LCA methodology.

1. INTRODUCTION

It is claimed that achieving sustainable development would bring immense benefits to organisations, governments and society through better environmental, economical and social development (Murphy and Drexage, 2010). However, sustainable development will not be achieved if climate change issues remain. The power to achieve sustainable development lies solely with governments who need to encourage business investments in low carbon technologies and green innovations. Internationally, governments are focusing on developing policies for organisations to address climate change issues. The strategies and policies are being developed especially for the energy-intensive industries (EIs) because they are one of the major contributors to GHG emissions. The iron and steel, the chemical, the petroleum, the pulp and paper, the pharmaceutical and the biotechnology industries are all EIs, and they are responsible for 45% of all business and public sector GHG emissions (Bullock, 2011; POST, 2012).

The biopharmaceutical industry focuses on healthcare, and it is an important part of the wider biotechnology industry (Mehta, 2008). This industry is a relatively new EI, and it is energy-intensive (Accenture, 2012). The biopharmaceutical industry employs biological processes to create useful commercial drugs such as monoclonal antibodies,

hormones, fusion proteins and vaccines through genetic manipulation of living organisms (Farid et al., 2008; Aggarwal, 2010). The biopharmaceutical industry is a fast growing industry with increased levels of production demand and a strong pipeline of drugs (Mehta, 2008). As the number of biologic drugs emerging from clinical development rises, manufacturers are now being prompted to find flexible, cost-efficient and environmentally feasible solutions for global scales of production.

The biopharmaceutical industry uses a range of manufacturing operations to achieve the exacting standards needed for drugs, run in either a traditional mode where equipment is cleaned in between batches or in single-use mode where no such cleaning is required (Farid et al., 2008; Sinclair et al., 2008). Traditional batch processing still remains the predominant approach to manufacturing with items largely constructed of stainless steel. Although the traditional manufacturing processes employing stainless steel equipment are well-established, several issues can be identified including high levels of water consumption (mainly for CIP and SIP operations), long process times and high capital investments (attributed to stainless steel equipment manufacture and assembly) (Mirasol, 2008). These issues are driving the industry to seek alternative manufacturing routes.

One such alternative relies upon the deployment of single-use technologies, which employ disposable equipment. Such single-use manufacturing process technologies can offer many benefits which include reduction in water consumption, reduction in the facility footprint, reduction in the high capital investment associated with stainless steel equipment, reduction in the frequency of process cross-contamination and process time reductions (Mirasol, 2008; Shukla and Gottschalk, 2012). Although single-use technologies can provide many benefits, there are several limitations associated with this type of manufacturing process. These include limited production scale (highest currently available volume of bioreactor is 2000 L), production of leachables and extractables by the single-use bags that could contaminate the product, potential adverse effects to the environment due to the increased solid waste levels inherent in operation with single-use components (Mirasol, 2008; Sinclair et al., 2008; European Commission, 2009; Eibl et al., 2010). Moreover, it is not clear how the environmental impacts of single-use items contribute to mitigating the consequences of normal operation using extensive water-based cleaning.

Whilst there are many established decision-support tools and methodologies to determine the process economics and efficiencies of alternative technologies and strategies, only limited information is known as to the environmental contributions of these manufacturing alternatives (Farid, 2007). It has been argued that the economics and efficiency aspects of the processes alone should not drive the biopharmaceutical industry's decision making process; the environmental aspects of processes must also influence the decision making process for an industry committed to improving the quality of human lives (Mauter, 2009).

The environmental decision-support tools for the biopharmaceutical industry can be developed using LCA methodology. The methodology is based upon a comprehensive analysis which estimates the cumulative environmental impacts of the process, product or activity, avoiding shifting of the environmental issues from one stage to another or from one media to another (Curran, 2006). The methodological framework developed by the International Organisation for Standardisation (ISO) to conduct LCA studies is widely adopted and consists of four phases: goal definition and scope, life cycle inventory analysis (LCI), life cycle impacts assessment (LCIA) and interpretation (Curran, 2006). Although other environmental tools such as Risk Assessment (RA), Material Flow Analysis (MEA), Technology Assessment (TA), and Environmental

Management System (EMS) exist, LCA is the only environmental tool that is process-orientated (Baumann and Tillman, 2009). It is also the only tool that can provide a comprehensive evaluation of the environmental burdens of a given manufacturing process without shifting the burdens from one phase/stage to another (Curran, 2006). These characteristics make LCA tools ideal for decision-support to aid decision-making processes when matched with similar tools for process selection and efficient waste management (Beaver, 2000).

This paper sets out the challenges associated with developing decision-support LCA tools for the biopharmaceutical industry. In the subsequent section of the paper, the challenges are elaborated and, where possible, recommendations are provided to address them effectively. These challenges may be relevant to many LCA efforts, however the focus of this paper is on the biopharmaceutical industry.

2. FOUR CHALLENGES OF DEVELOPING DECISION-SUPPORT TOOLS BASED ON LCA FOR THE BIOPHARMACEUTICAL INDUSTRY

It has been established that decision-support tools based on LCA are imperative for the biopharmaceutical industry as an aid to decision-making. Such decision-support LCA tools will allow the industry to select environmentally favourable manufacturing processes. However, there are four challenges that must be addressed before decision-support LCA tools can be successfully implemented in the industry. The challenges include; i) selecting the LCA system boundary for the manufacturing processes, ii) selecting the appropriate type of LCA approach for the decision-support tools, iii) obtaining the LCI inventory data, and iv) verifying the LCI inventory data. We shall now consider each in turn.

2.1 Selecting the LCA system boundary approach for the manufacturing processes

There are different LCA system boundary approaches that can be considered for a decision-support tool and they include; i) Cradle-to-grave, ii) Cradle-to-gate, and iii) Gate-to-gate. The cradle-to-grave LCA system boundary approach involves the evaluation of environmental impacts of a product/process from its raw material extraction and refining through component manufacturing, distribution, use and disposal at end-of-life (includes the supply-chain, use and end-of-life phases) (Pietrzykowski et al., 2011). In the cradle-to-gate LCA system boundary approach the evaluation of environmental impacts of a product/process from its raw material extraction and refining through component manufacturing, distribution and use (includes the supply-chain and use phases) is made. The cradle-to-gate LCA system boundary approach does not account for the end-of-life phase of a product/process (Kara et al., 2010). Finally the gate-to-gate LCA system boundary approach involves the evaluation of environmental impacts of a product/process during its use phase. The gate-to-gate LCA system boundary approach does not account for the supply-chain and end-of-life phases of a product/process (Puettmann and Wilson, 2005). Three schematic representations of the LCA system boundary approaches are provided (see Figs 1, 2 and 3 below). These schematic diagrams, based on a typical biopharmaceutical manufacturing process (monoclonal antibody manufacturing process), illustrate the differences between each system boundary approach.

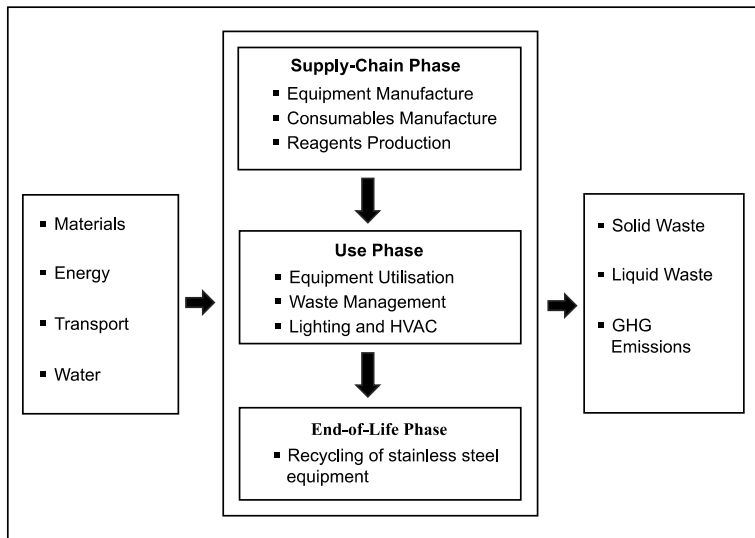


Figure 1. The LCA analysis of a monoclonal antibody manufacturing process using cradle-to-grave system boundary approach.

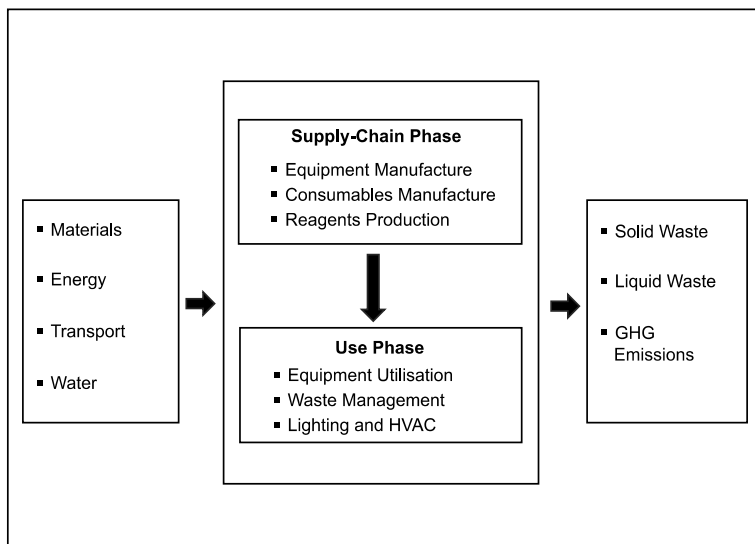


Figure 2. The LCA analysis of a monoclonal antibody manufacturing process using cradle-to-gate system boundary approach.

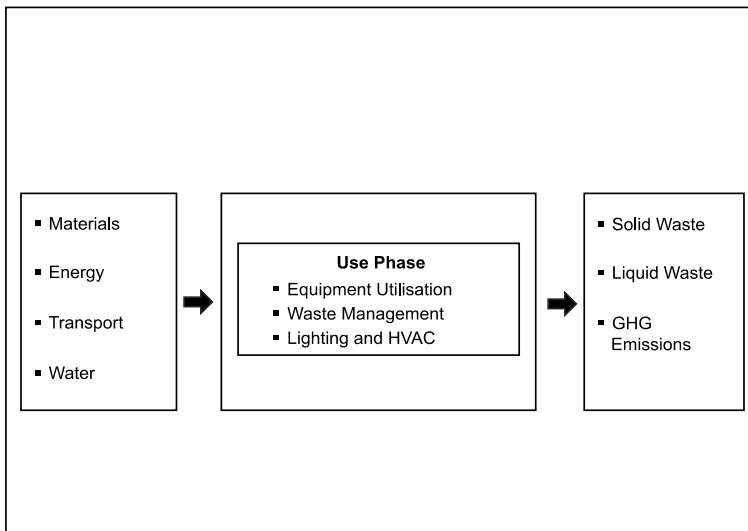


Figure 3. The LCA analysis of a monoclonal antibody manufacturing process using gate-to-gate system boundary approach.

Selecting the appropriate type of LCA system boundary for decision-support tools can be challenging as the current LCA methodologies and the standards set by the ISO create difficulties for defining system boundaries (Suh et al., 2003). It should be acknowledged that failure to define properly the system boundaries could cause the tools to be invalid (Matthews and Small, 2001). This is because important activities that may have huge impacts are not modeled by the decision-support tools. An LCA practitioner should analyse the objectives of a given study carefully and draw an initial system boundary. Further refinements should be made to the initial system boundary by including processes that are shown to be significant by sensitivity analysis (Suh et al., 2003).

2.2 Selecting the appropriate type of LCA approach for the decision-support tools

Consequential LCA (CLCA), Attributional LCA (ALCA) and Attributional LCA with system expansion are three different LCA approaches that aim to answer different questions, therefore the two LCA approaches must be distinguished (Finnveden, 2008). CLCA is an approach commonly used by decision makers where the main aim is to identify the cause and effect relationship between possible decisions and the environmental burdens (Mathiesen et al., 2009). ALCA is ideal for consumption-based accounting as it focuses on describing the environmentally relevant physical flows to and from a life cycle and its sub-systems (Finnveden, 2008). ACLCA with system expansion is a hybrid between ALCA and CLCA. The similarities and differences of the three LCA approaches are highlighted in Table 1. The choice of LCA approach should be based on the objectives and applications of a decision-support tool. This is because the appropriate LCA approach depends on the objectives of a decision-support tool (Finnveden et al., 2009).

Table 1. Characteristics of LCA approaches (Baumann and Tillman, 2009)

	ALCA	CLCA	ALCA with System Expansion
Choice of Data	Average	Marginal	Average
Allocation Procedure	Partitioning	System Expansion	System Expansion
Application	Consumption-Based Accounting	Change-Oriented LCA	Consumption-Based Accounting
System Subdivision	-	Foreground & Background	Foreground & Background

2.3 Obtaining the LCI data for biopharmaceutical processes & verifying the data

Obtaining the LCI data for a biopharmaceutical manufacturing process can be a challenge given the relative lack of experience with LCA in the industry. Unlike other industries, only limited numbers of biotech LCA studies exist and hence LCI data for biopharmaceutical processes are not readily available (Newman, 2010; Pietrzykowski et al., 2011; Mauter, 2009; Pietrzykowski et al., 2013). There are no databases specific to the biopharmaceutical industry, thus, data seeking for studies on biopharmaceutical processes can be laborious. This challenge could be addressed by using data from similar industries such as the chemical and pharmaceutical industries, by carrying out interviews with experts from the industry, and also by carrying out suitable literature surveys and analyses. A proper data collection procedure is needed and will help the industry to collect more easily the relevant LCI data needed for the decision-support tools development (Udo De Haes et al., 2002).

Upon obtaining the data, there is a need to verify the LCI data to determine their validity. This represents another challenge for the decision-support tools development. The biopharmaceutical industry lacks the methods needed to validate the data. However, the industry could respond to this challenge by again comparing the data with that from similar industries (e.g. chemical and pharmaceutical). This is possible because the manufacturing processes share common features (Mata et al., 2012). The industry could also validate the robustness of the LCI data by carrying out sensitivity and uncertainty analyses (Baumann and Tillman, 2009; Pietrzykowski et al., 2013). Sensitivity analyses evaluate how parameter choices affect the outcome of an LCA study (Pietrzykowski et al., 2013). They are used to identify the key parameters in a study that tend to affect the outcome of the study more than others (Pietrzykowski et al., 2013). Uncertainty analyses evaluate the effect of imprecise data on the outcome of an LCA study (Baumann and Tillman, 2009; Pietrzykowski et al., 2013). Data are considered to be imprecise because they can range over an interval (Baumann and Tillman, 2009). To carry out uncertainty analyses, all the varying data must be collected in order to establish interval and distribution (Baumann and Tillman, 2009). Once conducted the results of such analyses give further confidence in the prediction made

and hence of the value of the model to real-life decision-making.

3. CONCLUSIONS

Increasing pressure exerted by international governments on the EILs is driving these industries to reduce their environmental impacts. Industries such as the energy, automotive, chemical and pharmaceutical have been employing LCA to predict the environmental impacts of their processes, thus enabling these industries to implement engineering measures designed to reduce their impact, and in particular by employing low carbon technologies (Saur et al., 2006). The biopharmaceutical industry has been slow in carrying out LCA analyses. However, as the industry matures, the level of scrutiny placed on this industry by international governments will increase and hence, there is an urgent need for the industry to implement decision-support tools in their decision-making process.

LCA is an ideal methodology to be used by the industry as a basis for their decision-support tools. As an environmental management tool, these take into account all of the potential environmental impacts of a process, from resource extraction to final disposal (without shifting the impacts from one stage to another) (Mietinen and Hamalainen, 1997). Thus, this makes them ideal tools to be used as an aid to decision making in the biopharmaceutical industry.

The aim of the paper was to set out the challenges of developing decision-support LCA tools for the biopharmaceutical industry. The paper identifies that broader understanding of both the biopharmaceutical processes and of the relevant life cycle assessment methodologies are required for the successful development of decision-support LCA tools. The challenges identified should not be seen as hurdles to be cleared, but rather as learning opportunities for the industry. By addressing the challenges, the industry can move to a position where the manufacture of drugs is achieved in the most sustainable fashion. This will allow the industry to be a step closer towards achieving sustainability.

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