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Partnerships with the pharmaceutical industry to promote sustainability

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ABSTRACT: Rowan University has implemented unique project-based industrial partnerships for advancing sustainability in the pharmaceutical industry. Our project-based approach uses the Engineering Clinic model where junior, senior, Masters-level students partner with industry in applying green chemistry and engineering to improve the environmental profile of drug manufacture. Student teams have worked on several sustainability projects with three global pharmaceutical firms. These have resulted in students making recommendations that would reduce hazardous waste generation, greenhouse gas emissions, water use and energy consumption. The projects help guide industry in best available practices while students learn how to apply their green chemistry and engineering knowledge to an actual industrial case. The projects involve mentoring by both faculty and industrial partners.

INTRODUCTION

Rowan University has sought to improve on the concept of sustainability and green engineering education in a way that not only enhances student learning, and improves the environment. This is through integrating green topics in traditional courses [1][2] and through real-world projects in Rowan’s engineering clinic sequence where students are faced with industrial challenges [3][4]. The green engineering projects use a vertically integrated student team of junior, senior and master’s level engineering students who work with an industrial partner on approaches to pollution prevention. These projects provide an illustration of how companies can take advantage of universities in their region to assist in sustainable development and manufacturing. Student teams are able to learn about green engineering design and apply the principles of sustainable engineering (Table 1) directly to an actual industrial case. The industries involved partner by providing support in terms of senior staff, scientific/engineering process data, access to industrial facilities, and take initiatives to recommend process improvements.

Table 1: Principles of sustainable engineering [5].

1	Engineer processes and products holistically, use systems analysis, and integrate environmental impact assessment tools
2	Conserve and improve natural ecosystems while protecting human health and well-being
3	Use life cycle thinking in all engineering activities
4	Ensure that all material and energy inputs and outputs are as inherently safe and benign as possible
5	Minimise depletion of natural resources
6	Strive to prevent waste
7	Develop and apply engineering solutions, while being cognisant of local geography, aspirations and cultures
8	Create engineering solutions beyond current or dominant technologies; improve, innovate and invent (technologies) to achieve sustainability
9	Actively engage communities and stakeholders in development of engineering solutions

The role of academia on industrial projects is vital to infuse fresh ideas into manufacturing strategies. The students and industrial personnel gain experience through the project briefings and plant visits where an exchange of ideas is encouraged. Each project starts with seminars by each group on their particular area of expertise thus enhancing student learning and industrial outreach. Students are encouraged to be creative problem solvers and are mentored by both faculty and industrial partners. They are constantly challenged to look at the big picture and provide points of view that draw upon both principles learned in prior courses and sustainability concepts learned in the clinic experience.

This article describes the clinic projects at Rowan University that have focused on green engineering and sustainability in the pharmaceutical industry. This industry has a significant presence in our geographic region, where R&D, engineering, manufacturing, and environmental, health and safety (EHS) headquarters are located for many of the major global drug companies. These pharmaceutical manufacturing projects are co-funded by industry and the federal government (US Environmental Protection Agency, Region 2, Pollution Prevention Grants Program).

METHODS AND IMPLEMENTATION

The Engineering Clinic model used in carrying out these projects is a required course in our engineering programme. Students must register for two semesters (full year) of Junior Engineering Clinic and two semesters of Senior Engineering Clinic. In this project-based model, student teams are matched to each project based on their interest and expertise. Faculty advise the teams with input from the industrial sponsors on a regular basis. Before this can take place, faculty may spend months (and sometimes years) cultivating potential clinic project sponsors. The preliminary contact may take place at a conference, technical meeting or follow-up from another source. After initial contact, a visit is typically made by the faculty member to meet with the industrial sponsor and discuss the clinic programme, review capabilities and explore interest. Following a confidential disclosure agreement, more in-depth discussion may occur. Rowan University has a Clinic partnership agreement which is then modified and approved by both parties, before the project starts. One or more faculty members serve as project manager and co-project manager(s) and a liaison is usually assigned by the corporate sponsor who will be responsible for routine interactions with the student team.

At the beginning of the clinic project, students are presented with the problem from the industrial partner. They review the problem statement (overall goals) and translate that into project objectives for the year. They must present a project management workplan to the faculty showing the proposed tasks to be undertaken and target dates. At some point in the beginning of the semester, a meeting typically takes place involving the faculty, student team and the industrial liaison(s). This is helpful in reviewing the objectives, timeline, and procedures for the students to follow in interacting with various corporate constituencies, R&D, manufacturing, EHS, etc.

The clinic team then investigates the background of the project by reviewing process documentation provided by the corporate partner and performing a literature search. These activities result in a comprehensive review of background information (patents, publications, etc) and previous strategies and solutions for similar industrial cases. Although this is a common part to almost any engineering project, the literature search benefits the students by allowing them to become more familiar with the unique background of the topic. For example, pharmaceutical engineering is not typically taught in undergraduate chemical engineering programmes, so the students must understand the terminology and processes used in drug manufacture.

As the project becomes more clearly defined, students will recommend alternative solutions based on the literature review and design criteria. Technical feasibility and transferability to the pharmaceutical industry (drug manufacturing regulations) are primary concerns. The advice from the industrial liaison is crucial in understanding US Food & Drug Administration Current Good Manufacturing Practices (FDA cGMP) regulations regarding process changes. Environmental and economic concerns (operating and capital expenses) are then considered for each of the design alternatives. Industry then provides feedback to the students regarding their recommendations and after making appropriate revisions, students will then ensure that their *greener* solutions are optimised. This takes place in the lab or with detailed calculations and simulations. The learning experience for the students is to see how industry prioritises alternative strategies.

The deliverables on the project are a mid-term and final design report, and presentations to the industrial sponsors. It is through these vehicles, that a significant amount of learning takes place. Students submit memos on a weekly basis that summarise their activities in the period and plans for the subsequent week. Monthly telephone conference calls are usually done with the industrial partner. The mid-term report serves as an important way to keep the industrial partner informed of the progress and as a way for them to comment on specific aspects of the project and its direction. It also serves as a method for faculty to provide feedback on student writing skills. Final report and presentation are delivered at the end of the year. Draft reports are revised by faculty advisors and returned to students. In addition to the detailed presentations to the industrial partner, presentations are also typically given at professional society meetings. These aspects of our engineering clinic programme help improve student communications skills in a substantial way. The active participation of the industrial partner, e.g. providing technical information and feedback to the student team, at all stages during the semester is invaluable to the success of the project.

Through the final report and presentation, student teams try to sell their idea(s) to the industrial partner. But, it is up to the project liaison to recommend the green proposal to their management. Students evaluate the environmental impact of the project based on several parameters. They compare the *base* case versus the green improvement. First they determine the raw materials reduced, waste reduced and energy saved for the process improvement. If the process to be improved will be scaled up at some future time, an estimate of the impact on annual production is then made for the proposed scale of implementation. For example, a pilot process to produce 100 kg of API will be scaled-up to manufacture 100 metric tons (100,000 kg) of API when the drug is manufactured on a commercial scale. The students then evaluate the emissions saved through evaluating the life cycle impact of the improvement. This involves the analysis of the *cradle* to *grave* of the pharmaceutical manufacturing process. This life style thinking is crucial to the development of an engineer since they need to understand the broader implications of their design in terms of raw materials and energy consumed at all stages of development.

Through the use of life cycle assessment (LCA) software (SimaPro® 7.2, PRé Consultants, Amersfoort, Netherlands; and EcoSolvent®, Safety and Environmental Group, Zurich, Switzerland) students can quantify the amounts of raw materials, emissions, and energy saved in process modifications. This is done through developing life cycle inventories for the *cradle* of solvent manufacture, in-process use in the pharmaceutical synthesis, and the *grave* of solvent waste incineration. SimaPro® is used to estimate emissions from raw material manufacture and energy generation and EcoSolvent® is used to estimate emissions from waste disposal (incineration). The impact of process modifications on the overall environment (e.g., reduction in green house gas (GHG) emissions in energy generation) can also be determined through the LCA software which can provide information on specific emissions such as metric tons of CO_2.

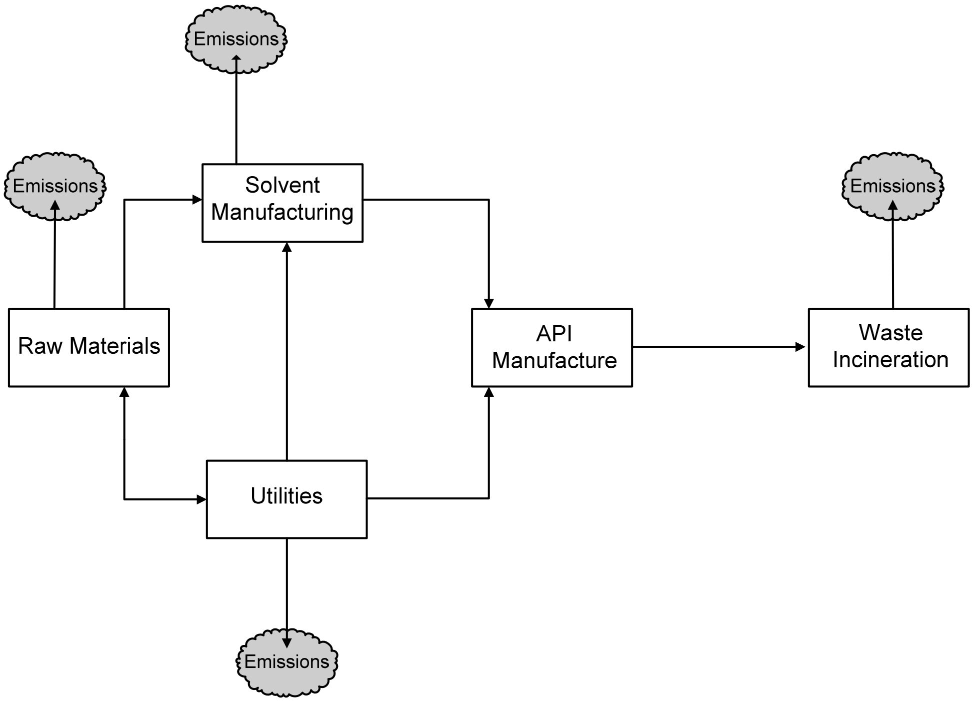

Figure 1: Emissions sources produced during the life cycle for solvent used in pharmaceutical manufacturing (Adapted from Ref [6]).

The use of life cycle thinking in making decisions in the design process is a unique way of approaching engineering education for the next generation of engineers. In the past, green engineering was not a high priority, but the corporate climate has shifted towards viewing sustainable practices as a key component in business decisions. There are also many economic benefits in greener processing solutions if they are integrated appropriately. For this reason, it is believed that the next generation of engineer needs to be knowledgeable in environmental design tools, such as LCA software, and have experience in design case studies involving green alternatives.

RESULTS AND DISCUSSION

The majority of our projects with the pharmaceutical industry have focused on solvent reduction strategies and how they can be implemented to improve the environmental footprint of drug production. Through our research in this field, we have found this to be an area of mutual interest by faculty at Rowan and by the pharmaceutical industry in general. Solvents are a major contributor to the emissions profile in manufacturing the active pharmaceutical ingredient (API) used in drug formulations. The studies have shown that they have a significant impact on the environment from direct use in synthesising the API and more broadly when evaluating the life cycle of the solvent [7-9].

The first green engineering in the pharmaceutical industry project started in 2005 with Bristol-Myers Squibb (New Brunswick, New Jersey). Over the past five years the authors have worked on projects with R&D and manufacturing facilities at Bristol-Myers Squibb, Novartis (East Hanover, New Jersey) and Pfizer (Peapack, New Jersey; New York, New York; Barceloneta, Puerto Rico; Kalamazoo, Michigan) and continue to seek out additional partners for the clinic programme. These projects all have similar structure and overall focus. Some of the common elements of these projects and specific outcomes of some of the projects are described below.

The theme of solvent reduction and recovery has been present in most of our engineering clinic projects and links nicely with many of the sustainability principles mentioned in Table 1. These projects also lend themselves nicely to allowing students to evaluate both environmental and economic impacts, since data is readily available on most solvent systems used in the pharmaceutical industry. The project with Bristol-Myers Squibb investigated the use of a hybrid pervaporation-constant volume distillation operation for the recovery of the solvent, tetrahydrofuran, in the production of a new oncology drug [10][11]. This analysis was successfully performed on the pilot-scale since the drug is still in development. The case study with Novartis investigated a fixed bed adsorption process to reduce methanol and water usage in a Heck coupling reaction step in a drug synthesis [12]. This process is also being conducted on the pilot scale.

One of the projects with Pfizer examined how solvent recovery could be integrated into a drug manufacturing process already on a commercial scale [13-15]. This project explored the integration of distillation and pervaporation for the recovery of the solvent, isopropanol, from the manufacture of celecoxib, the active ingredient in the arthritis pain medicine, Celebrex®. This project successfully showed how solvent recovery operations can be implemented on a commercial scale and the environmental and economic benefits. A second project with Pfizer has examined the recovery of various solvents using a multi-purpose distillation system for smaller volume lots of solvent waste from one of their plants [16]. In all case studies, these green design strategies were compared to the base case of solvent incineration and resulting reductions in solvent use and green house emissions determined using a life cycle assessment. Details of the design of the greener solvent recovery and/or reduction systems are available in the referenced papers.

Developing a partnership with industry is the most important facet of a clinic project. Therefore, from a university standpoint, a *champion* for green engineering at that company who also believes in the benefit of partnering with academia is vital for success. The companies mentioned above have green chemistry/engineering teams, and we have benefited by developing relationships with particular engineers who then make a case to their division or the *green* committee for the projects. The projects must also be matched to faculty and student expertise. Projects should be of a level of technical difficulty that a group of advance undergraduates and masters students could achieve outcomes within an academic year.

Additionally, sufficient resources need to be allocated. This includes both financial support from the industrial partner and/or funding agency along with the time commitment of industry and academic personnel to guide the student team. Realistic timelines and expectations need to be agreed upon. Undergraduate teams work on a semester model: 16 weeks from September through December and start-up again for another 16 weeks from January through May. The focus of the project should be narrow enough so that the team can obtain the necessary background and start formulating a plan of action, so that preliminary results can be obtained after the first semester. These preliminary results are conducive to *mid-course* adjustments to the workplan that can be made through mutual agreement between the faculty and industrial liaison.

Reasonable confidentiality/intellectual property agreements should be negotiated to allow faculty and students to present some aspects of their work at conferences. It is recognised that the student teams may be working with confidential formulas, batch records, or other information that needs to be kept secret. A review clause in the agreement allows faculty and students to have the ability to present non-confidential aspect of their work so that they can compete in student paper competitions and for faculty to present at professional society conferences or publish in journals. In the case with Bristol-Myers Squibb, neither the name of the new oncology drug or specific process chemistry is revealed. In other cases, results may be reported on a different scale (or basis) or as percent reduction in a particular performance parameter (instead of giving an exact amount). Finally, the projects should be able to be *mapped* to academic department goals, mission or accreditation needs. Schools in the United States following ABET criteria would find these projects are excellent vehicles to evaluate student outcomes in several of the criterion.

CONCLUSIONS AND FUTURE PLANS

Projects that focus on green engineering approaches in pharmaceutical manufacture have been conducted by student teams in the Rowan University Engineering Clinic programme. These real-world projects have led to recommendations to improve the carbon footprint of pharmaceutical syntheses by reducing solvent use. The projects benefit academia and industry since there is an exchange of green engineering ideas through the year leading to quantifiable outcomes. Our recommendations in the above mentioned projects would result in the reduction of 2.01×10^7 kg/yr emissions (1.81×10^7 kg/yr of CO_2) and save 7.56×10^6 USD/yr. New engineers are graduating with knowledge in green engineering practices and how to apply them in an industrial setting. Students gain an understanding of pharmaceutical industry culture and important steps in drug manufacture. Faculty develop expertise to advance state-of-the-art in green engineering for future projects. We have already had numerous follow-up discussions with the industry from the press releases and papers presented at conferences.

In 2009, the US Environmental Protection Agency presented Rowan University with an Environmental Quality Award for Environmental Education for *assist(ing) the pharmaceutical industry in Region 2 in source reduction, pollution prevention, and green engineering design through the use of an innovative engineering clinic outreach program led by Drs. C. Stewart Slater and Mariano Savelski* [17]. As a publically-supported college of engineering, we are fulfilling our mission of not only educating the next generation of engineers, but preparing them to assist in the economic development of the region in a sustainable way.

Currently, we are developing software tools for the pharmaceutical industry to use in evaluating the feasibility of implementing alternative greener process technologies. These will enable engineers to have the capability to quickly evaluate solvent recovery processes based on both life cycle emissions reduction and economic recovery potential. Future plans are to continue to extend our partnership activities and seek opportunities where green chemistry and engineering can be applied to reduce the carbon footprint of manufacturing. This has the potential to impact other industrial sectors and all activities from research through commercialisation.

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