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Energy Savings in Pharmaceutical Facilities: A Risk-Based Approach

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This article provides an in-depth look at the general risk profiles in the pharmaceutical industry and evaluates the place of energy saving features within the context of risk management.

Introduction

Recent escalations in energy prices have prompted pharmaceutical companies to review their operating costs. When energy costs were lower, energy saving features had a much longer return on investments and accordingly, there was less incentive to incorporate them. The risk of compromising the reliability and integrity of the system has been cited to avoid the use of many energy saving schemes, energy saving devices, and new and innovative energy-efficient design. Even five to 10 years ago, many companies and engineers did not consider using variable speed drives even though they had excellent financial paybacks, due to problems in the field.[3] There is a renewed effort in the industry to reduce energy usage, partly because of extremely high energy cost and partly because of the desire to be more environmentally friendly with sustainable design and green buildings. It is a perfect time to revisit some of the so-called "sacred" and "traditional" criteria and requirements that have limited use of energy efficient designs in the past.

With the above background, it is high time to examine whether the industry has been too risk-averse and reluctant to follow basic principles of energy management and sustainable design. Practices such as green design, carbon mapping, sustainable design, etc. are being discussed everywhere, and are becoming more mainstream.[4] In many countries, there are stringent Green House Gas (GHG) emission regulations and there is no doubt that very soon all industries will be faced with increasing pressure on sustainability. The pharmaceutical industry has to develop a balanced approach to energy savings and sustainable design versus risk mitigation. We must start the process now.

Risk Profiles of the Pharmaceutical Industry

The pharmaceutical industry, as a whole, is a very conservative group. The pressure of conforming to stated and sometimes unstated requirements of government regulating agencies like the US FDA, European Union, and regulators of other countries have created an atmosphere of minimal innovation and more of "doing it the same way" attitude. Trying out new methods, even if it achieves the same result, is often considered too risky. This article will review the various elements of risks that are generally encountered by the pharmaceutical industry.

Drug Product Safety

The educated consumer expects that all drug products are manufactured in the safest way that is humanly possible. The stakes are very high. So, it is understandable that the FDA and European agencies are extremely concerned about the process, the environment, and the SOP related to manufacturing medicines. Predictably, the pharmaceutical industry has taken a very conservative stance so that the risk of product contamination or product failure is perceived as practically eliminated.

Personnel Safety

In addition to ensuring the safety of drug products, another area of risk for the pharmaceutical companies is the human exposure to certain chemicals during the manufacturing process. Most of the current drug products are made from manipulations and handling of various combinations of chemicals. A number of formulations require the use of solvents. Also, during the research and development stages of drug development, a variety of chemicals and agents are used that could pose threats to personnel if exposed. Biological agents with

The pharmaceutical industry, like many other industries, is feeling the pressure to reduce the cost of goods and lately has turned its attention to energy efficiency to help meet their goals.[1] However, unlike the other industries, the pharmaceutical industry is heavily regulated and modifications and improvements should undergo a risk assessment prior to implementation. The concept of "risked-based" analysis is not new to the industry, and as a result, decisions on energy saving features can not simply be a financial decision. The decision also must ensure that the systems, equipment, or design is reliable and will not compromise the very essence of drug efficacy and drug safety.

The intent of this article is to give an in-depth look into the general risk profiles of the pharmaceutical industry, and assess the place of energy saving features within the context of risk management. A quantitative methodology has been proposed to consider all the elements affecting the use of energy saving features, including the risk element. This methodology can be a useful tool in making decisions on energy saving opportunities and sustainable design, as more and more pressures from society is put on all industries. Detail ed discussions on various energy opportunities have been purposely avoided as there are plenty of articles and seminars which have addressed them. However, certain applications and opportunities of energy management have been discussed only to exemplify base issues on risk versus applications.

various degrees of biohazard levels (BL-1 thru BL-4) are routinely used in the research. Recently, there has been tremendous increase in the use of "potent" and "cyto-toxic" compounds. Most of these chemicals are highly toxic and must be contained. Sensitizing compounds such as penicillin and cephalosporin have such adverse effects that they are typically manufactured in dedicated facilities. Government agencies such as OSHA have guidelines for the exposure limits and "right to know" laws.

Environmental Implications

These chemicals also pose threats to the environment. Release of these chemicals in the air or in wastes (solids and liquids) must be minimized. In the United States, the Environmental Protection Agency (EPA) provides guidelines and regulations for any release of such pollutants to the atmosphere. The pharmaceutical companies have the added responsibility to be "environmentally friendly."

Reliability

In terms of risk management, the concern of reliability in the manufacturing or R&D facilities is an important issue which often comes into play in the pharmaceutical industry. Certain design elements are deemed too risky as it may compromise reliability of the plants. Some of the issues are real, for example, ensuring almost "zero-failure" for long term pre-clinical studies. At the same time, criticality of some of the issues are sometimes over-emphasized. An example would be sizing the cooling and heating systems for manufacturing facilities to the maximum capacity required for extreme ambient conditions so that manufacturing operation is not interrupted at any time. In most cases, the unit operations of a batch manufacturing process can be interrupted with a little planning. This practice of sizing for the worst condition unduly increases the sizes of chillers and boilers; and, if not properly selected, will function very inefficiently most of its life span. Another example would be to design the air handling systems for coaters and fluid bed granulators for the worst ambient conditions when these pieces of equipment are not operated continuously. Is it not possible to ride through a "four-hour" peak condition and not operate the equipment at that time? In some cases, the answer is yes; but no one wants to analyze the risk and make that decision.

Currently, the facility design decisions are heavily weighed to support a low risk tolerance of the industry. Interestingly, there are only a handful of written requirements from regulatory agencies which actually affect the design. However, there are traditions based on "unwritten" rules which have created an environment of fear of the unknown, resulting in repetitive design concepts without much thought toward innovation.

Energy Usage in Pharmaceutical Industry

The pharmaceutical industry consumes on average about $1 billion of energy annually.[2] This staggering figure gives us an idea of the potential savings that can be achieved by focusing more attention to the energy usages. Figure 1 illustrates how the energy usage has been escalating consistently.

The process of drug making consists of several discreet steps starting from discovery research to pre-clinical testing, clinical manufacturing to bulk active substance manufacturing, and then to formulations/finishing facility. In addition, there are needs for warehousing and administrative offices to support the drug discovery and drug manufacturing. These functions, facilities, and processes vary widely and have very different energy requirements and usages. Figures 2 and 3 are illustrations of how energy consumptions in such facilities vary. These charts also show a typical breakdown of energy usages between the various user categories such as processes, lighting, and Heating, Ventilating, and Air-Conditioning (HVAC).

Energy Cost Savings

Due to the recent surge in energy prices, every company is looking for ways to reduce energy consumption and lower the energy bill. There are two distinctly separate ways of saving energy costs. One is the energy procurement management and the other is the energy user side management. Energy procurement management consists of reviewing energy procurement contracts and finding ways to reduce the supply side rate structure or suggest alternate procurement methods. Another way is to use plant resources (such as waste) to

provide energy sources for the facility. Cogeneration, captive power generation using various types of turbines, etc. are some of the ways to reduce operating costs.

The energy user side management may include peak demand management, such as peak shaving with the use of on-site generators during peak loading, thermal storage, etc. But the primary focus of user side management is to reduce energy consumptions of various plant users like HVAC, lighting, processes, and operations. Investigations of these Energy Conservation Opportunities (ECOs) form the basis of most of the energy saving and green building discussions. Based on the illustrations above, the largest opportunities are in the HVAC field, which includes generation and distribution of central utilities such as chilled water systems, steam systems, compressed air systems etc. However, the ECOs are not limited to HVAC and lighting. Process, critical utilities, and operating philosophy of a facility also have a significant effect on energy consumption, and must be investigated. Examples of this category would be re-use of reject water from Reverse Osmosis (RO) systems, efficient use of hot and cold WFI systems, re-use of dumped water from purified water or WFI systems, etc. It should be noted that these energy conservation features often present risks to the company in a certain way, whether on product safety, personnel safety, reliability, or other issues.

Risk versus Energy Savings

Over the years, there have been several misapplications of energy recovery systems, which have added fuel to the notion of unreliability and risky applications in terms of energy saving features. The authors have knowledge of two facilities, which installed rotary air-to-air heat recovery system, but were soon abandoned for the fear of exhaust air being entrapped in the rotary energy wheel and getting mixed with the fresh air. There are many other examples of misapplications which have added to the apprehension of using energy saving features. We often find that energy engineers who are not familiar with the pharmaceutical industry recommend energy saving features that compromise the current Good Manufacturing Practice (cGMP) or Good Engineering Practice (GEP) associated with the pharmaceutical world. Even the usual energy saving opportunities commonly practiced in other industries must be reviewed carefully and critically for the specialized application of the pharmaceutical industry. On the other hand, the pharmaceutical industry itself has become very conservative and does not accept something that may present a hint of risk to the operation. Consequently, the industry has been consistently making the most conservative decisions on energy features. Some examples of such conservative decisions are:

1. 100% Outside Air (OA) versus re-circulated air for multi-product manufacturing facilities – *product safety*
2. 100% OA versus re-circulated air for Labs – *personnel safety*
3. High Purity Water Systems – Hot USP or hot WFI; Cold WFI; how to cool; heat it back – *inefficient design is accepted to avoid validation issues*
4. Micro environment – isolators in aseptic facility in non-potent applications; ventilated cages in animal facilities – *rarely thought of in terms of energy saving feature*
5. Room Classifications for solid dosage spaces – *overkill for the ease of compliance*
6. Air change rates versus room classifications – *Still using the vertical laminar flow techniques when the semi-conductor industry has changed the way clean spaces are designed - afraid to change*
7. Chilled water temperature reset – *rarely done*
8. Air handling unit discharge temperature reset – *rarely done*

Item #	Energy Conservation Opportunities	Energy Saving Potential			Initial Cost of Installation			Environmental Effect			Controllability			Risk Factor			Total	Remarks
		Importance Factor	Score	Weighted Score	Importance Factor	Score	Weighted Score	Importance Factor	Score	Weighted Score	Importance Factor	Score	Weighted Score	Importance Factor	Score	Weighted Score		
1	Change the current 100% OA system to recirculated system for a multi-product solid dosage manufacturing facility.	2	4	8	-1	2	-2	1	3	3	-2	2	-4	-4	1	-4	1	Acceptable
1 alternate	Change the current 100% OA system to recirculated system for a multi-product solid dosage manufacturing facility.	2	4	8	-1	2	-2	1	3	3	-2	2	-4	-4	2	-8	-3	Not Acceptable
2	Lower air change rate for Grade B clean rooms in a Sterile Facility	2	4	8	-1	-1	1	1	1	1	-2	0	0	-4	4	-16	-6	Not Acceptable
3	Lower air change rate for Grade C clean rooms in a Sterile Facility	2	3	6	-1	-1	1	1	1	1	-2	0	0	-4	2	-8	0	May be Acceptable
4	Unoccupied Mode in terms of temperature, RH and air change for Processing Rooms	2	3	6	-1	1	-1	1	2	2	-2	0	0	-4	2	-8	-1	May be Acceptable
4 alternate	Unoccupied Mode in terms of temperature, RH and air change for Processing Rooms	2	3	6	-1	1	-1	1	1	1	-2	0	0	-4	3	-12	-6	Not Acceptable
5	Remove room classification & Lower air change rates in a Solid Dosage Facility	2	2	4	-1	0	0	1	1	1	-2	0	0	-4	1	-4	1	Acceptable
6	Reuse reject from Animal Drinking water Reverse Osmosis (RO) system for Large Animal Trench washing in a Vivarium	2	2	4	-1	2	-2	1	3	3	-2	1	-2	-4	0	0	3	Acceptable
7	Reset of Chilled Water Temperature during relatively lower ambient conditions	2	2	4	-1	0	0	1	1	1	-2	0	0	-4	1	-4	1	Acceptable
8	Reset of Discharge Air Temperature for air handling units serving Manufacturing Rooms	2	2	4	-1	0	0	1	1	1	-2	0	0	-4	3	-12	-7	Not Acceptable
9	Reset of Discharge Air Temperature for air handling units serving Laboratory & Lab support spaces	2	2	4	-1	0	0	1	1	1	-2	0	0	-4	1	-4	1	Acceptable
10	Use of economizer control in air handling units serving manufacturing spaces with critical pressurization requirements.	2	3	6	-1	1	-1	1	1	1	-2	0	0	-4	3	-12	-6	Not Acceptable

Table A. Examples of quantitative analysis of energy conservation opportunities.

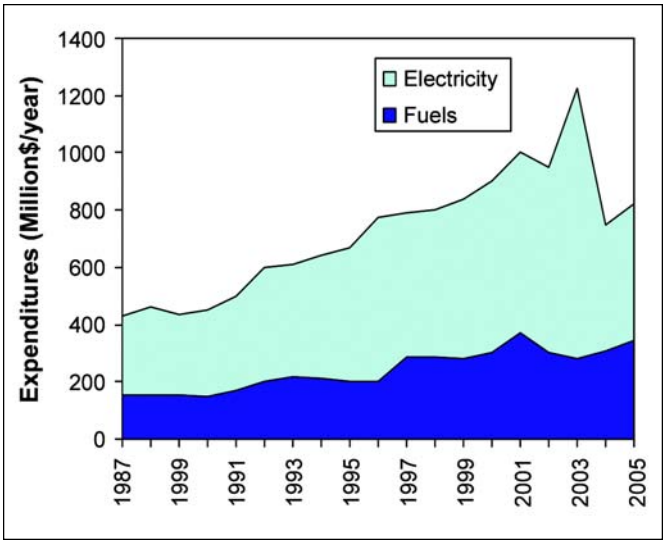

Figure 1. Historical energy expenditures of the US pharmaceutical industry. (Source: US Census)

9. Night setback for process rooms – *rarely done due to validation issues*
10. Lower face velocity or vortex controlled fume hoods – *still considered too risky by many*

Energy and Environments

Most energy related projects directly or indirectly affect the environment. In many cases, energy recovery or saving features are equated to reduced environmental discharge or emission. In addition to the usual NOx, CO, particulate matters, and other listed emission limitations, there has recently been a lot of discussion on greenhouse gases. Carbon dioxide is a major source of greenhouse effect, and most likely, will shortly be listed as a pollutant. Most multinational companies are already reporting their carbon footprint. The other companies are considering implementation of the "carbon mapping" program to monitor and perhaps control CO2 discharge. In most cases, the energy saving features will have a direct impact on carbon footprint. This is an important side advantage of energy saving features and must be considered in the evaluation of ECOs.

Evaluation Methodology Using Quantitative Analysis

As noted in the previous discussions, the energy saving features may have direct impacts on several important areas, including adding risks to the process, reliability, safety, and environment, etc. Each of the affected areas may have different importance and sensitivity to the project, company, or the industry. The evaluation must consider all of these aspects with varying importance or significance. The following is a suggested methodology that can be used for the decision making process. It is suggested that this is done before a true Return On Investment (ROI) analysis is conducted. The ROI analyses can take considerable engineering time and effort. Instead, a more judgmental analysis can be done to filter out most of the energy saving candidates. The full ROI analysis then can be performed for the energy saving candidates that pass the first scrutiny.

It should be noted that there are several energy conservation items that add little or no risk to the business. Examples are Low-E glass, additional insulations, white roofs, high efficiency, and energy star rated equipment, etc. These "non-risk" energy conservation opportunities do not need to pass through the above stated methodology of filtering the risk elements of various ECOs.

Methodology

The following describes the methodology for risk analysis of the energy conservation opportunities:

A. The significant areas (categories) affected by energy saving features:
   a. Risk to product, personnel, facility, reliability, etc.
   b. Energy Saving Potential
   c. Installation Cost
   d. Environmental Effect – positive or negative
   e. Constructability – in an existing condition

   Note: There may be a few other categories such as "maintenance" that can be added to the list, but the above five categories are by far the most significant in the decision making process.

B. Importance factor or weight of each category: An Importance Factor (IF) must be assigned for each of the affected area. For example:
   a. Risk Factor: IF = (-)4
   b. Energy Saving Potential: IF = 2
   c. Installation Cost: IF = (-)1
   d. Environmental Effect: IF = 1
   e. Constructability: IF = (-)2

C. Score: Assign scores for each ECO under each category. The scores could be assigned based on a scale as follows:
   a. Risk Factor: Score between 0 to 4: 0 when there is no risk; 1 when it is low risk; 4 is when it very high risk.
   b. Energy Saving Potential: Score between 1 to 4: 1 means low savings and 4 means high savings.
   c. Installation Cost: Score between (-)1 to 4: (-)1 means reduced installation cost; (+)1 means low installation cost and 4 means high cost.
   d. Environmental Effect: Score between (-)1 to (+)4: (-)1 for being negative or adverse impact; 0 would mean no impact; (+)4 means high positive impact.

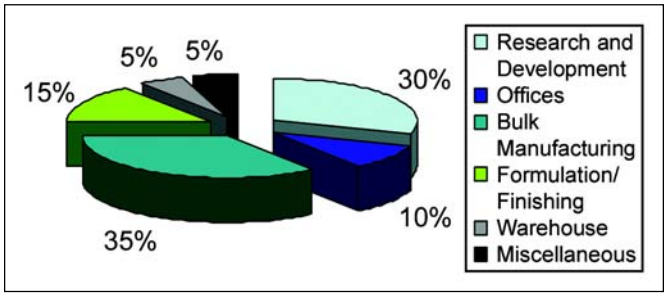

Figure 2. Breakdown of energy usages within pharmaceutical sector.[2]

e. Constructability: Score between 1 to 4: 1 for easy installation and 4 for difficult installation.

D. Assigning Scores: It is extremely important to assign scores properly. As with any numeric analysis such as this, the scores should be established with well thought out logistics and not picked arbitrarily. As is evident from the above, risks to product or personnel have the highest importance factor of 4. So, the score assigned to risk factor has a great effect on the outcome or result of the analysis. Table A gives examples of how to assign scores for risk factors.

E. Total Weighted Score: Total weighted score is the summation of each weighted score under each category which is derived by multiplying the assigned score with the weight, i.e., the importance factor.

F. Decision Making Process: Decision can be made based on the total cumulative score for each ECO. Higher positive total weighted score will signify better expected result with high ROI, low environmental impact, and most importantly low risk. Low cumulative weighted score or negative total score will signify higher risk or low ROI and should be discarded. The high scoring ECOs should then be pursued further to calculate the actual ROI and justified through financial benefits.

Table A shows some examples to illustrate the methodology. The actual weight and scores should be adjusted based on the actual situation, risk taking profile of the company, local environmental limitations, etc.

Suggested Implementation Program

It is important to develop a solid program to plan, evaluate, and implement various energy saving ideas. In most cases, the program will require significant investments on the part of the company. Usually, there is a minimum ROI that a company expects before the spending is approved. However, as pointed out here, many of the opportunities have additional benefits such as reduction in emission, including lowering of carbon footprint, sustainable design, etc., which go beyond just the ROI filter.

The implementation plan should follow the following logistics:

New Facility

1. Energy use should always be on the table during the design phase as well as construction phase. There should be an energy budget during the initial design phase.
2. Perform a risk-based study similar to the methodology suggested in this article.
3. Ensure the energy saving features that passed the initial test is considered and applied during the design phase. Often, energy savings features are easy targets for value engineering.

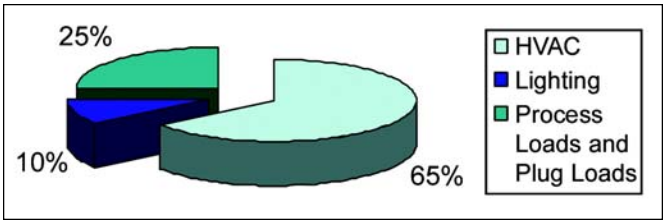

Figure 3. Typical energy consumption breakdown.[2]

Existing Facility

1. Implement an energy audit.
2. Make sure you hire capable engineers who understand both energy saving ideas as well as the type of pharmaceutical facility under audit.
3. Make sure the audit is comprehensive and includes process based systems and energy consuming operations.
4. Expect the firm to go beyond the "norm" in the pharmaceutical industry, within the constraints and boundaries of cGMP and GEP regulations in identifying energy saving potentials.
5. Perform a risk-based study for implementing the energy saving candidates, similar to the methodology suggested in this article. The client must be involved in this risk-mitigated analysis of energy candidates, and must be responsible for the decisions.
6. Based on the initial assessment, the ECOs with higher positive total scores (passing through the initial filter) should be analyzed further for actual ROI.
7. Implement the ECOs with reasonable ROI.
8. Measurements: It is important to have a baseline before the implementation of any energy saving opportunities. Have another measurement of energy consumption after the implementation. However, it is tricky as a large number of energy saving opportunities are influenced by the outside (ambient) environment, which is not controllable. Also, a high numbers of ECOs are dependent on a combination of situations and environments that are difficult to duplicate.

Conclusion

The time has come to revisit the system design and philosophies traditionally used in the pharmaceutical industry. The high cost of energy has given impetus to this movement. FDA and other agencies are also much more flexible with their new "21st century initiatives" and "Risk-Based Approach" subset for compliance and conformance. In addition, the industry collectively has the responsibility to ensure the sustainability of our environment. We need to join the "green" movement without sacrificing the efficacy and safety of the medicinal products. This article is intended to merely give ideas on how we can evaluate each scenario objectively and make the correct decisions. It is too easy to say that the industry is restricted and bound by all the compliance regulations, and there is no scope to save energy and become "greener."

At the same time, it should be realized that this industry is not suited for "overzealous" energy engineers to direct energy saving programs without understanding the risk. The

authors strongly agree that there is an opportunity to achieve reduced energy usage and balance energy savings and the various risks associated with making drug products. The decisions to implement energy saving opportunities must be made with proper engineering knowledge, risk assessments, and financial considerations instead of "it does not work" or "it is too risky" statements.

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