External Manufacturing EHS Best Practices
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Introduction

The industry trend towards outsourcing manufacturing continues to expand throughout international business operations. In particular, the chemical and pharmaceutical contract manufacturing businesses have seen rapid growth over the past decade. This significant change in the traditional manufacturing model has created some unique challenges from an Environmental Health and Safety (EHS) and risk management perspective. This business relationship involves a Client or company requesting the toll and a company providing the toll manufacturing services which are commonly referred to as:

- Contract manufacturer
- Contract processor
- Custom chemical manufacturer
- External contract manufacturer
- Outsourced manufacturer
- Supplier of outside services
- Third party service provider
- Toll processor
- Toller

For the purpose of this paper, the term “External Manufacturer” (EM) will be used. This paper will provide an overview of some of the current best practices which have been developed for external manufacturing for both the Chemical and Pharmaceutical industries.

Chemical Industry Best Practices

The American Institute of Chemical Engineers (AIChE) Center for Chemical Process Safety (CCPS) published the Guidelines for Process Safety in Outsourced Manufacturing Operations (reference 1) in 2000. The techniques presented in this book are targeted to help improve performance in:

- Safety
- Industrial (occupational) hygiene
- Catastrophic incident prevention
- Off-site and on-site environmental responsibilities
- Quality production and packaging of contracted materials

Addressing the combination of these five elements adds assurance that external manufacturing will be performed in a safe, efficient and environmentally sound manner. This guideline is organized into the following chapters:

- The Toller Selection Process
- Mutual Agreements, Obligations, and Contract Considerations
- Pre-Startup and Startup Activities

- Ongoing Operations: Audits and Follow-up
- Closure and Audit

One of the key challenge areas is defining the right balance in the relationship between the Client and the EM. Table 1 from this guideline summarizes potential pitfalls to be addressed when defining these joint responsibilities for a successful Client/EM partnership.

Table 1: Potential Problems Encountered with External Manufacturing Relationships

Potential Problems for External Manufacturers	**Potential Problems for Clients**
Communication breakdown with the client	Communication breakdown with the external manufacturer
Contract termination is an economic threat	Less control over the process than when it is done in-house
Must rely on certain information provided by the client	Environmental issues due to unknown hazards from other ongoing tolls or a toller's past or current practices
Safety issues due to unknown or insufficient information on processing hazards by the client	Safety issues due to operating and maintenance practices by the toller Agency actions or catastrophic events at the toller's facility can threaten supply chain
For new tolls, dealing with an unknown company	For new tolls, dealing with an unknown toller
Uncertain wear and tear on equipment by unfamiliar materials or processing techniques	Uncertain management practices by the toller
Non-contractual transfer of expertise to client	Confidentiality concerns for proprietary information
Identifying cross-contamination problems between previous and successive products and processes	Receiving product contaminated by other products and processes
Timing issues due to scheduling multiple products or batches	Timing issues due to a more complex supply chain
Late receipt of raw materials or packaging from the client	Personnel turnover can create unforeseen delays

This guideline also provides several example EM EHS forms and checklists such as a sample Pre-assessment Questionnaire, and a sample EHS Assessment checklist including a sample Quantitative Assessment Format. The use of these types of supporting EHS evaluation tools could help the Client evaluate the potential EM facility's ability to:

- Protect human health and the environment,
- Prevent business interruption, and
- Prevent possible loss of public confidence as a result of manufacturing the products(s).

Pharmaceutical Perspectives

The Pharmaceutical Supply Chain Initiative (PSCI) is a group of major pharmaceutical companies created to facilitate pharmaceutical suppliers consistent operation with industry expectations about labor, health and safety, environment, ethics and management systems. The Business for Social Responsibility (BSR) is the facilitator and project manager for the PSCI. As a first step, the PSCI created the Pharmaceutical Industry Principles for Responsible Supply Chain Management ("the Principles") in 2007. These Principles address five areas of business practices throughout the pharmaceutical industry supply chain including ethics, labor, health and safety, environment and related management systems. The PSCI developed a supporting Guidance Document (Reference 2) in 2007, which provides examples on meeting these expectations. The five key areas for which this guidance document also provides sample program elements include:

1) Management Systems
    a. Commitment and Accountability
    b. Legal and Customer Requirements
    c. Risk Management
    d. Documentation
    e. Training and Competency
    f. Continual Improvement

2) Ethics
    a. Business Integrity and Fair Competition
    b. Identification of Concerns
    c. Animal Welfare
    d. Privacy

3) Labor
    a. Freely Chosen Employment
    b. Child Labor and Young Workers
    c. Non-Discrimination
    d. Fair Treatment
    e. Wages
    f. Freedom of Association

4) Health and Safety
    a. Worker Protection
    b. Process Safety
    c. Emergency Preparedness and Response
    d. Hazard Information

5) Environment
    a. Environmental Authorizations
    b. Waste and Emissions
    c. Spills and Releases

More detailed information on PSCI Guidance Documents can be found at www.pharmaceuticalsupplychain.org. Several of these supporting resources are currently offered in multiple languages (e.g. English, Spanish, Portuguese and Chinese).

Example Pharmaceutical Company EM EHS Practices

A certain pharmaceutical company has offered the following red flags to be wary of when visiting an EM (in particular in a developing economy).(Reference 3) They suggested it is best to keep your "eyes always open" for potential red flags such as:

- You are not allowed to see the EM's manufacturing processes.
- You are not allowed to see the workers' living quarters.
- Exits are chained or bolted closed.
- Workers appear to be very young.
- Your eyes, nose or throat are burning from odors, fumes or particles in the air.
- There are no signs of an emergency alarm system.
- Workers are on high ladders, scaffolds or roofs without guards or protection.
- Waste appears to be dumped on site.
- Surface water onsite is oily, discoloured or contains dead fish.
- Soil onsite is oily, stained or vegetation is dead or discoloured (not due to seasonal changes.

If a red flag is observed, this company recommends bringing it to the attention of the facility management, asking clarifying questions if necessary and reporting it to the appropriate technical staff in your organization. Depending on the nature of the observation and the EM's response, you may decide to initiate an onsite audit.

Another key concept shared in this paper is the "EHS Maturity Ladder Concept," which categorizes a Client's EMs into one of three levels including:

1) Minimum Requirements – basic awareness and protection (legal compliance)
2) Manage Risk to Supply Chain – assess and control risk
3) Partner/Nice to have – mature and integrated benchmarking (continuous improvement)

This categorization provides an effective means for ranking EMs and helping them strive for continuous EHS improvement.

Certain pharmaceutical companies have established Standards for Responsible External Manufacturing, including online resources for suppliers. Some of the key EHS performance measures being tracked related to EMs include the following:

- Percentage of Client contract language which includes EHS requirements
- Percentage of Client EMs that have had an assessment (broken down for both new and existing EMs)
- Percentage of Client EMs rated as Repeat Marginal or Unacceptable

Another pharmaceutical company who is a member of the PSCI projects that EMs will provide up to 35% of the volume of their manufacturing needs. As of mid-2008, they have inspected 100% of the potential EMs for new business and found certain of these to be unacceptable due to EHS issues and received completed surveys from approximately 85% of their existing EMs. Starting in 2009, existing EMs will be inspected to achieve compliance with the PSCI principles on a three to four year schedule with the highest risk suppliers

evaluated first and most frequently. When concerns arise from either EM responses or site visits, they work with the EM to understand the issue, establish an improvement plan and offer technical support if necessary to enable the EM to achieve the required standards. If an existing EM does not show adequate improvement over a period of time, they may seek alternative suppliers or discontinue work with the original EM.

Another pharmaceutical company who is also a member of the PSCI, claims to have developed a formal EHS Sourcing program. The goals of this program include:

- To adhere to internal standards for the engagement of contract manufacturers and researchers, assuring they have sufficient resources and systems to avoid or mitigate potential EHS impacts arising from the activities conducted.

- To conduct EHS assessments for contract manufacturers and researchers (CMRs), key suppliers, and logistic centers prior to outsourcing activities.

- To perform subsequent EHS supplier reviews on a routine basis assuring performance has been maintained and is acceptable.

- To improve the EHS competencies of our contract manufacturers and key suppliers through our training and coaching.

- To engage with other pharmaceutical companies to help our suppliers implement the Pharmaceutical Industry Principles for Responsible Supply Chain Management.

- To integrate EHS criteria into our decision-making for the purchase of goods and services

The company's claimed results include:

- Conducted 140 on-site EHS supplier review assessments at the facilities of contract manufacturers and researchers, key suppliers, and outsourced logistic centers in 2007.
- Performed an additional 27 follow-up reviews for suppliers currently contracted.
- Provided coaching sessions in 2007 for 19 of our key suppliers, often in local languages, enhancing EHS competencies to improve performance.
- Performed on-site general safety and fundamental industrial hygiene training to six suppliers in China, as a follow-up to comprehensive technical training conducted in 2006.

Potent Compound Handling Capability and an Independent Certification Option

Pharmaceutical EMs which handle higher hazard Active Pharmaceutical Ingredients (APIs), include those considered to be occupationally potent compounds (i.e. APIs with Occupational Exposure Limits (OELs) less than 10 µg/m³). These EMs have a critical need to have the right "hardware" (facilities, equipment and engineering controls) and "software" (programs, practices and procedures) to protect personnel and the environment (reference 4). Typical elements of a Potent Compound safety program may include:

1. Review of the potential hazards associated with Pharmaceutical Drug Substances and Drug Products – recognizing the hazard
2. "Tools" to evaluate and measure exposure – evaluation of the hazard and risks
3. Containment and controls appropriate for the risk presented by the hazard – risk reduction
4. Standard Operating Procedures (SOPs) for potent APIs or products
5. Training programs in potent compound awareness
6. A determination of the environmental impact of the Drug Substance or Drug Product and associated manufacturing processes

Failure to manage these risks effectively can potentially cause delays in time to market, lost revenue for the drug innovator and EM, damage to the business relationship, decreased workforce confidence and potential liability.

Pursuing an independent certification for a critical EHS program area such as a Pharmaceutical EM's potent compound safety program effectiveness can be a win-win for both the Client and the EM. The Client gets an unbiased assessment of an EM's potent compound handling capability while the EM can get recognition as being qualified to handle potent compounds which in turn benefits their marketing and sales efforts.

One recognized example is the SafeBridge® Certification program (reference 5) which assesses the strengths and weaknesses of the systems, programs and facilities in the area of worker protection. The process utilizes a 60-point assessment criteria and scoring system developed by SafeBridge Consultants, Inc. health and safety professionals. This certification process has several phases including:

- Phase 1 – Pre-visit questionnaire completion
- Phase 2 – On-Site Assessment which reviews overall Program Management, Hazard Evaluation, Containment and Controls, and Communication
- Phase 3 – Summary Report and Grading

A minimum overall score of 65% must be achieved with none of the four program areas under 55% to receive a Letter of Certification. An overall score of 80% would qualify as an industry leader. The SafeBridge certification is a unique and recognized system for evaluating the safe handling and production of highly potent APIs.

Summary and Lessons Learned

This paper has provided examples of current EM EHS management practices available in the Chemical and Pharmaceutical industries. In particular, practices from the AIChE CCPS, PSCI and Potent Compound Safety program evaluation and a certification option were described. This information should provide a valuable roadmap and resource for companies in the process of developing an EM EHS program. Key lessons learned from recent experience developing a Company's EM EHS program include:

- EHS should be a pro-active team member on your company's strategic EM partner selection process team.
- Select EHS training resources should be shared with your EMs (e.g. combustible dust hazard awareness).
- Pursue Company membership in leading industry groups (e.g. AIChE CCPS, PSCI, European Process Safety Centre) to gain, share and maintain an awareness of industry EHS best practices.

References

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4) Ader, Allan W., Mason, Justin, J., and Farris, John P., 2007, Important elements in evaluating contract manufacturing organizations in the handling of "potent" active pharmaceutical ingredients and products, Chemistry Today, March/April 2007

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