Cost Reduction of Solvent Recovery in Pharmaceutical Plants

Process Gas Chromatograph MAXUM II replaces costly Lab Analysis by on-line Analytics

Case Study · August 2008

Use of Solvents

The pharmaceutical industry relies on the use of large quantities of organic solvents in a great number of manufacturing steps including chemical synthesis, fermentation, extraction, formulation and finishing of products. Solvents such as acetone, methyl ethyl ketone and tetrahydrofuran are commonly used as reaction media and for extracting products in the pharmaceutical, specialty chemicals and fragrance industries. Other solvents frequently encountered include hexane, dichloromethane, methanol, ethyl acetate, toluene, xylene, triethylamine, butyl acetate and isopropanol.

Solvent Recovery

Solvent disposal costs and VOC emissions control have been primary concerns in the industry for some time. For various reasons, there is an increasing interest in recovering solvents with the direct cost saving being one of the strongest arguments. In some processes with intensive solvent use, the cost of the solvent can be a significant proportion of the overall product cost.

Another compelling reason for recovering solvents is the increasing environmental legislation against emissions; such emissions may be as a result of a process design where solvent recovery was not incorporated at the outset, or where venting has occurred as a result of plant problems. With increasing commercial and regulatory pressures on pharmaceutical industries, the recovery, reconditioning and reuse of solvents is an important aspect of running production facilities efficiently. Further, the FDA initiative "Pharmaceutical Manufacturing in the 21st Century" - with its goal of optimizing production processes so that quality becomes an integral element of the process - marks a crucial turning point.
Batch distillation
The most popular method of recovering solvents is filtration and distillation. Alternatively, carbon bed absorbers are occasionally used for filtration, and steam is then used to desorb and recapture the solvents. The disadvantage of this technique is that water is introduced into the recovered solvents and this must be removed before they can be reused. A batch distillation process is therefore employed to purify the solvent to an acceptable level for reuse.

Clearly, there is no advantage in purifying the solvent beyond the required level as this would represent wasted resources, so analyzers such as the MAXUM II process gas chromatograph are used to give an accurate, reliable, continuous online measurement of the concentration of solvents.

Challenge
Use of solvents for production processes can be expensive - expensive to purchase, expensive to store and expensive to dispose. Further, as oil prices continue to rise, so will also costs for oil-based solvents. Solvent recovery provides cost savings by reducing the purchase costs of new solvents, reductions in waste handling costs and reductions in storage costs of both solvent and wastes.

Hence, solvent recovery processes are increasingly used with analyzers to monitor and optimize the processes by providing accurate data about the actual grade of purity achieved.

A large pharmaceutical company approached Siemens with a solvent recovery application encompassing 7 different batch distillation processes as listed in Table 1.

The analyzer requirements for this demanding analysis objective were

- Capability to serve all 7 batch processes (Table 1) with a single analyzer only
- High analytical performance regarding analysis time, choice of detectors, column technology, etc.
- High reliability in operation
- Seamless integration of the analyzer into the plant production process
- Seamless integration of the analyzer into the plants communication network

Solution
Process vs. laboratory analysis
Siemens recommended to solving this application by means of on-line Process Analytical Technology (PAT) instead of laboratory analysis equipment as commonly used. Compared with laboratory testing of samples, on-line analysis can provide the facility with faster results, improved accuracy, and allows trends to be monitored in real time. On-line solvent recovery analysis is likely to reduce the number of batches that are rejected, saving both time and money.

Consequently, process gas chromatography is increasingly used in the Pharmaceutical Industry to measure solvent concentrations from recovery and/or distillation processes.

Indeed, even critical measurements of solvent concentration levels to the ppb range are achievable, when required.

MAXUM II, the ideal solution provider
Most solvent recovery processes are done in batches, often encompassing several different solvents at various intervals. To be an effective solvent recovery process monitor, the gas chromatograph must accommodate this scenario. The MAXUM II PGC (Fig. 1) does this with ease: A single MAXUM analyzer can accommodate several methods as well as several hardware applications.

MAXUM provides

- Multiple detectors, multiple columns and multiple valve arrangements
- The software capability to control several batch methods
- The capability to communicate analysis results per batch

Thus, MAXUM is the ideal solution provider for monitoring solvent recovery processes as shown in Fig. 2.

MAXUM edition II
MAXUM edition II is a universal process gas chromatograph offering an outstanding broad variety of analytical possibilities. Main application field is process monitoring and control for gases and vaporable liquids in rough industrial environments. MAXUM II performs a wide range of duties in refineries and chemical/petrochemical industries. MAXUM II features e. g. a flexible, energy saving single or dual oven concept, valveless sampling and column switching, and parallel chromatography using multiple single trains as well as a wide range of detectors such as TCD, FID, FPD, PDHID, PDECD and PDPID.

Important user benefits include

- Flexible range of oven capabilities
- Multiple detector and valve options
- Local panel and remote workstation
- Powerful software
- Extensive local and remote I/O’s and serial links
- Multiple network capabilities
- Large, experienced support team

Fig. 1: MAXUM II Process Gas Chromatograph
The Siemens solution (Fig. 2) comprises:

- One MAXUM Process Gas Chromatograph in split airbath oven configuration
- One sample gas stream
- Three straight forward analysis trains with sample and column switching valves and two FIDs and one TCD.
- 7 analytical methods using EZChrom software to handle the 7 different batch processes

This configuration enables MAXUM to measure simultaneously Methanol, Ethanol, Ethyl Acetate, Tetrahydrofuran, Toluene, Total Alcohols (train with FID 1), H2O (train with TCD) and Methylene Chloride, Isopropanol, Isooctane, Acetone (train with FID 2). Consequently, the recovery processes of all 7 solvents (Fig. 2) can be monitored and controlled with just one analyzer and without any modification of the analyzer.

Fig. 3 shows examples of the analytical performance of MAXUM.

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**Table 1: Specification summary of the seven solvents to be analyzed during recovery**

<table>
<thead>
<tr>
<th>Solvent to be Recovered</th>
<th>Solv. conc. % min</th>
<th>H2O % w/v max</th>
<th>MeOH % max</th>
<th>MeCl2 % max</th>
<th>Toluene % max</th>
<th>Total Alcoh. % max</th>
<th>EtOH % max</th>
<th>THF % max</th>
<th>EtOAc % max</th>
<th>Iso Octane % max</th>
<th>Non Volatiles ppm max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetrahydrofuran (Process A)</td>
<td>99.0</td>
<td>0.05</td>
<td>0.02</td>
<td>1.0</td>
<td>2.0</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Acetone</td>
<td>98.5</td>
<td>1.0</td>
<td>0.5</td>
<td>6.0</td>
<td>0.1</td>
<td>0.1</td>
<td>0.5</td>
<td>0.3</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimethylformamide</td>
<td>99.6</td>
<td>0.1</td>
<td>0.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylene Chloride</td>
<td>99.1</td>
<td>0.13</td>
<td>0.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethyl Acetate</td>
<td>99.0</td>
<td>0.1</td>
<td>6.0</td>
<td>0.7</td>
<td>0.3</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetrahydrofuran (Process B)</td>
<td>99.3</td>
<td>0.03</td>
<td>5.0</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toluene</td>
<td>99.0</td>
<td>0.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

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Fig. 3 shows examples of the analytical performance of MAXUM.
User Benefits

Process analyzers in a Pharmaceutical plant contribute significantly to a correct, efficient and safe plant operation. The analyzers must be of very high performance and reliability, and their integration into the plant requires a high degree of know-how and engineering experience. Siemens has brought these attributes to industry for many years.

In the actual application, the end-user found the following benefits resulted from use of the MAXUM Process Gas Chromatograph in their solvent recovery process:

- Capability to monitor and control seven different solvent recovery processes with just one single Chromatograph and without hardware or software modifications
- Reduced costs per measurement due to reduced lab operations
- Improved process through-put due to much faster response from on-line process analysis compared to lab analysis
- Reduced costs by avoiding re-running of distillation processes through critical point analysis.
- Improved solvent yields through better and faster process monitoring
- Reduced waste solvent with need for disposal

Compared to the conventional method of analyzing samples off-line in the laboratory the end-user estimated a total annual savings due to the installation of MAXUM of above $200,000 (Table 2).

<table>
<thead>
<tr>
<th>Process</th>
<th>Frequency</th>
<th>Per batch</th>
<th>Assumptions</th>
<th>Savings per batch</th>
<th>Annual savings estimated (50 batches)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved process through-put (Avoid delay waiting on lab data)</td>
<td>Increase number of batch distillations by 2.0 % for same facility</td>
<td></td>
<td>Facility capital costs to be $ 500K</td>
<td>$ 10 000</td>
<td></td>
</tr>
<tr>
<td>Reduced costs per measurement (Lab operations)</td>
<td>Per batch</td>
<td>1.5 h</td>
<td>Hourly lab/capital rate to be $ 275</td>
<td>$ 412</td>
<td>$ 20 600</td>
</tr>
<tr>
<td>Avoidance of re-run distillation by missing cut-off point. Critical point determination</td>
<td>Re-run assumed to occur twice per 50 batches</td>
<td></td>
<td>Single distillation costs to be $ 15 000</td>
<td>$ 30 000</td>
<td></td>
</tr>
<tr>
<td>Improved solvent yields through better and faster process monitoring</td>
<td>Per batch</td>
<td></td>
<td>Yield increase by 10 % 10 % yield improvement equal to 100 gallon solvent</td>
<td>100 gal solvent − $3 000</td>
<td>$ 150 000</td>
</tr>
<tr>
<td>Reduced solvent waste for disposal</td>
<td>Per batch</td>
<td></td>
<td>Reduced waste solvent by 10 % 10 % yield improvement equal to 100 gallon waste solvent</td>
<td>Disposal costs − $ 0.36 per gallon</td>
<td>$ 1 750</td>
</tr>
<tr>
<td>Total Annual Costs Savings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$ 212 350</td>
</tr>
</tbody>
</table>

Table 2: Savings summary

The information provided in this case study contains descriptions or characteristics of performance which in case of actual use do not always apply as described or which may change as a result of further development of the products. An obligation to provide the respective characteristics shall only exist if expressly agreed in the terms of contract. Availability and technical specifications are subject to change without notice. All product designations may be trademarks or product names of Siemens AG or supplier companies whose use by third parties for their own purposes could violate the rights of the owners.

Fig. 4: Typical solvent recovery plant