Enhanced Process Safety
During Centrifuge Inertization

A leading global supplier of generic pharmaceuticals was able to enhance process safety and operational efficiency during centrifugation by using a METTLER TOLEDO oxygen gas measurement system.

In a market that is affected by constant price pressure, process optimization is a key factor for profitability. METTLER TOLEDO offers measurement systems to provide enhanced process safety and efficiency in pharmaceutical processes.

Limiting oxygen concentration
The last step in the production of high-enriched penicillin entails centrifugation of the product to enable further processing to final drugs. Centrifuges play a key role in separating penicillin from water and organic solvents to obtain purified penicillin crystals. Safety and efficiency must always be given top priority in this separation process. To eliminate the risk of explosion, an inert nitrogen gas atmosphere serves to limit the oxygen concentration in the centrifuge. Consequently, the headspace is permanently purged by nitrogen. The INGOLD oxygen measurement system ensures that the limiting oxygen concentration (LOC) is constantly maintained, minimizing the consumption of nitrogen gas at the same time.

Precise oxygen measurements
During the separation of penicillin crystals from a mixture of water, ethyl and isopropyl alcohol, entry of air into the centrifuge has to be inhibited. If the oxygen concentration level exceeds 8%, then staff and equipment are dangerously exposed to explosion hazards. Through a pre-determined
feed of nitrogen, the oxygen concentration should be limited to below 2 Vol-%. The excess of an upper limit of 6.5 % causes immediate centrifuge shut-down.

On the other hand, pharmaceutical process equipment has to fulfill strict hygienic design requirements to ensure protection against product contamination. In addition, the whole centrifuge including measurement equipment is exposed to frequent cleaning cycles, requiring the use of fully sterilizable oxygen sensors.

**Previously handling of application**

Originally, this application was controlled by applying a constant, nitrogen overpressure. Expensive micro fuel cell systems were used to monitor the oxygen concentration in each centrifuge. These systems always required a costly and maintenance-intensive gas sampling conditioning system consisting of pump, cooler and filter to ensure reliable measurements. Sampling systems were subject to failures causing expensive damage to the micro fuel cell oxygen system. Such short-comings resulted in repairs and process standstills. Consequently, production capacity was reduced.

**METTLER TOLEDO solution**

Such negative experiences caused the top-ten generic manufacturer to install a METTLER TOLEDO oxygen measurement system consisting of an oxygen sensor InPro 6800 G, a retractable housing InTrac797 e, and the oxygen transmitter M700. In an initial step, the system was set up in parallel to the existing installation. In this instance however, conditioning of the measurement gas became superfluous and the sensor was built directly into the centrifuge headspace. Comparison of the systems showed excellent measurement correlation, but a more detailed analysis resulted into several benefits from the METTLER TOLEDO solution.

**Customer-benefits**

- Exclusion of risks of penicillin contamination through unhygienic bypass gas sampling system.
- Saving of huge cost of upkeep of gas sampling system and micro fuel cell.
- Improved response time and accuracy as a result of true in-line measurement.
- Elimination of oxygen diffusion caused by long gas-sampling tubing.
- Four-week maintenance and calibration cycle for oxygen sensor InPro 6800 G proved sufficient.
- Use of InTrac 797 e retractable housing with sterile double rinsing chamber permitted sensor maintenance without interrupting centrifugation process.
- Simplification of regular sensor checks in air. Continuous and efficient production guaranteed.

**Additional savings in operation costs**

The customer was able not only to significantly increase process safety, but also to increase yield. The newly applied solution offers further potential for savings in operating costs, in particular for nitrogen gas consumption.

Therefore oxygen measurement is used to control nitrogen flow into the headspace of the centrifuge, while a minimum calculated flow guarantees absolute process safety at oxygen levels below 7 %. Typically, oxygen concentration is controlled to lie between 3 to 5 Vol-% oxygen. With this enhanced control concept, the centrifuge headspace is no longer purged with nitrogen more than absolutely necessary. Beforehand, the process was controlled by constantly applying nitrogen at a sizeable over-pressure. The oxygen measurement value dropped to 0.5 Vol-%, causing excessive nitrogen consumption. Inert gas consumption can be drastically reduced by optimum control of the centrifuge inertization process, resulting in reduced operating costs.
The measuring system from METTLER TOLEDO
Accuracy and low maintenance of continuous oxygen measurement systems require a sensor that is robust, fast in response and resistant to moisture as well as to destruction by solvents. User-friendly operator interface and means of communication with external control and monitoring systems are also both a must. Retractable housings offer the ability to insert or retract the sensor from a continuous process at will without interrupting production. Versions with pneumatic retraction as well as inductive position indicators are also available.

Advanced cleaning systems allow the oxygen measuring sensor to be calibrated automatically on a timed basis using air as calibration gas.

**O₂ sensor InPro 6800 G**
- Easy two-minute maintenance
- Microorganisms cannot adhere to the sensor surface due to the enhanced finish (N5 / Ra16 Quality)
- Fully sterilizable and autoclavable
- For hazardous areas (gas and dust)
- ATEX / FM
- VarioPin (VP) connector (IP 68)

**Retractable housing InTrac 777 e**
- Ability to retract sensor during continuous process operation
- Supports maintenance of O₂ sensor
- Approved for use in hazardous areas
- ATEX

**Transmitter O₂ M700 XC**
- Easy installation and operation
- Polished stainless steel for hygienic applications
- Simultaneous monitoring of oxygen and temperature
- Redundant measurements with one transmitter
- Approved for use in hazardous areas
- ATEX / FM

METTLER TOLEDO offers the complete measuring loop required for reliable measurement tasks in hazardous areas.

For more information:

www.mt.com/o2-gas