

Centrifuges, Stirrers & Shakers

GMP Environments Require Centrifugation that Supports Compliance

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Food manufacturers, pharmaceutical companies and biotech firms involved in the manufacture and testing of active raw materials must adhere to the stringent guidelines required of Good Manufacturing Practice (GMP) environments. Countries such as the US, EU and Japan are signatories to the International Conference on Harmonization (ICH) which in 1999 published 'GMPs for Active Pharmaceutical Ingredients'. This also applies to countries such as Australia, Canada and Singapore which also adopt ICH guidelines.

These guidelines are integral to maintaining quality control. They lay down the minimum requirements that a manufacturer must meet to ensure products are of consistent high quality and do not present any risk to consumers or general public. The World Health Organization (WHO) version of GMP is used by pharmaceutical regulators and the pharmaceutical industry in over one hundred countries worldwide, primarily in the developing world. The European Union and the FDA enforces similar requirements to the WHO GMP.

Many manufacturers rely on the high throughput performance of floor-standing ultracentrifuges and high-performance centrifuges to help increase their productivity. They demand more throughput, faster turns, and greater control over workflow. However, instruments that are run in GMP environments must also actively support compliance. Two key compliance features focus on security levels and traceability. Manufacturers are also looking for high-performance instruments which offer innovative features that support GMP compliance while eliminating much of the burdensome administrative work that compliance entails.

Bespoke Security Access Restrictions

Relieving the admin burden imposed by GMP compliance is important as regulatory authorities must be certain that the compliance data submitted by manufacturers is a consistent, reproducible and accurate reflection of production. This is especially important when assessing the hazards and risks to users, consumers and third parties, including the environment.

Controlling access to equipment within a GMP environment is therefore critical. Security levels provide the ability to control the level of access each user has to the centrifuge. Password protection with an option to select a PIN expiration date provides optimum security. Administrators may require log-in before anyone can use the centrifuge. Being able to restrict operators to running only certain pre-defined programs further limits the potential for errors. Systems such as Beckman Coulter Life Sciences' Optima XPN and Avanti JXN Series centrifuges feature password protection for up to 50 unique user profiles. They are then assigned one of three security levels - Administrator, Super User, or Operator. The latter can be further restricted to run only certain pre-defined programs, limiting the potential for errors.

- Administrator: Unlimited access
- Super User: permission to run all programs, manage users, assign programs. Some systems like the Optima XPN also enable the Super User to manage the rotor library
- Operator: permission to run assigned programs and change user options.

Crucial Data Logging Parameters for Traceability

Extended traceability is essential to meet the increasingly stringent GMP quality requirements. Offering a powerful tracking capability helps maintain an audit trail of centrifuge activities by ensuring that data from each and every run is recorded and linked to a specific user.

To enable manufacturers to build a detailed archive of each run, Beckman Coulter has set down 10 core data logging protocols that customers should expect from ultra and high-performance centrifuges to support compliance:

- User information
- Start date and time of the run
- End date and time of the run
- Rotor type
- Program name
- Acceleration and deceleration parameters
- Before run comment
- After run comment
- Detailed information about each step in a run (speed, RCF, time, temp, $\omega 2t$)
- Any diagnostics that occurred during the run
- Graph of the run (speed and temperature)
- Electronic signature (if enabled)

The above information should be stored and viewable on the centrifuge itself, and easily exported to a USB drive, network drive, or printer for archiving.

Enhanced Data Tracking for Reproducibility Validation

- Free-form comments
- System and program log
- Electronic signature
- Extended user-defined protocols
- Real-time run graphing
- Rotor tracking also by serial number
- Remote monitoring and control
- Email diagnostic alerts

Alongside the standard centrifuge run parameters, it is useful to have a run-log history that enables the lab to capture user comments entered before or after a specific run. This can be especially helpful when issues arise which affect reproducibility. These comment fields can include batch numbers, the name of the product being manufactured, an occurrence during the run that is in any way out of the ordinary, or anything else related to the run that would be useful to store in the log for future reference. An additional feature offered by the Optima XPN and Avanti JXN Series centrifuges allows the user to add free-form comments before and after the run using the on-screen keyboard

Instruments should offer both a 'system log' - a list of the dates and responsible users whenever a system option has been modified - and 'program log'. The latter contains the history of changes to a particular run program including the date, time and user responsible for each program modification.

Early Warning System for Rotor Tracking

In addition to capturing and storing run data, the electronic signature capability adds additional traceability once a centrifuge run is complete. An electronic signature representing the run log's author, reviewer, or approver can then be applied to the record. The electronic signature should include the user's name, date and time stamp, the instrument serial number, and any notes that were entered at the time of signature.

Another enhanced feature - real-time run graphing - offers a visual way of tracking and recording the actual speed and temperature during the centrifuge run. The information can then be stored in the run log for future reference. This quickly helps to identify any variation in speed or temperature. In addition, being able to track the number of cycles accumulated on specific rotors helps maintain laboratory safety and maximise the productive life of the instrument. Once set up, users can choose rotors by serial number from an onscreen rotor library. The centrifuge tracks the number of cycles, so the life of the rotor can be precisely tracked and retired before it becomes unsafe and potentially causes damage to the centrifuge or lab personnel.

Setting up and using user-defined protocols helps ensure consistency between runs and minimises user error during the run setup. Depending on the complexity and level of detail they offer, user-defined programs should be able to ensure that virtually any protocol can be set up and stored for future use.

With the Optima XPN and Avanti JXN Series a lab has the ability to program names of up to 64 characters (any combination of letters, numbers, or symbols), so they can assign secure but memorable names for easy recall. The centrifuges allow up to 1,000 user-defined programs, consisting of up to 30 steps each, to be assigned to specific operators, making it possible to limit the number of users with access to the protocol.

Flexible, Remote Working

Most bio production facilities contain more than one centrifuge. The ability to remotely monitor and control the capabilities of these instruments adds greater flexibility to workflow, particularly if it can alert them early of problems which might affect uptime. Users can check the status of all instruments from virtually anywhere via a personal computer using Virtual Network Computing (VNC) software.

In addition, with Beckman Coulter's MobileFuge application (for the Optima XPN and Avanti JXN Series) users can use their smart phone or tablet to monitor the performance and workflow of up to 16 centrifuges at any one time. The MobileFuge, which is available for iOS and Android devices, enables researchers not only to remotely monitor their instruments but to have basic control over them.

Currently, Beckman Coulter is the only centrifuge company which offers this level of network connectivity. It taps into the potential of mobile technology to provide customers with a new and more efficient way of working by extending certain vital functions of the lab to wherever researchers are based, and in whatever time zone.

Another feature on the centrifuge which supports remote working and enables early intervention is the ability to send email diagnostic alerts whenever there is an issue. Once designated users have been identified and their contact details entered into the system, as soon as a diagnostic issue occurs, the centrifuge will send an electronic notification to everyone on the list alerting them to the problem.

Compliance to Ensure Product Quality

Beckman Coulter has been at the forefront of centrifuge innovation since the first commercial ultracentrifuge (Model E Ultracentrifuge) was introduced in 1947. This was later used in research to isolate the polio virus and to confirm the structure of DNA. Even then, it could operate to 60,000 rpms and an intricate photo-optical system permitted researchers to chart separation of samples under forces as high as 256,000g.

GMP compliance is designed to put product quality first, reduce risk and improve overall standards. Globally, regulatory authorities continue to seek greater collaboration to streamline GMP inspections internationally, enabling more manufacturers to be monitored, while avoiding duplicate inspections. This places ever more stringent obligations on biotech, food and pharmaceutical companies. In turn, they look to instrument manufacturers such as Beckman Coulter to provide them with systems which both support compliance and minimise the administrative hassle involved.

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