

Single-use Technology: How to Overcome Existing Limits

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On behalf of biotechnet Switzerland

The Zurich University of Applied Sciences (ZHAW) in Wädenswil has become the 'single-use Mecca' of the highly dynamic branch of biopharmaceutical manufacturing. On June 3 and 4, researchers, process engineers and specialists in apparatus engineering and facility design met at the BioTech 2013 conference to discuss the latest developments in single-use technology (SUT), to push back the existing limits and to explore the potential of future trends in this domain.

As single-use process solutions become increasingly established not only in clinical applications, but also in the commercial production of biological drugs (e.g. seed inoculum production) and in critical process applications, the users of SU solutions have to rely more and more on the quality system and supply chain management of their vendors. "At Sartorius, we have invested a lot of effort in recent years in further developing our quality system, supplier relationship and own biological competence to ensure security of supply, robust quality and suitability of the SU bag or bioreactor for its intended application", comments Dr. Christel Fenge, Vice President Marketing & Product Management Fermentation Technologies at Sartorius Stedim Biotech. "In this context, I would like to especially mention our strategic collaboration with Südpack, a leading film extrusion company, and resin suppliers that has allowed us to implement a Quality by Design approach to raw materials, film extrusion, assembly and gamma irradiation to assess and control their impact on final product suitability for the application." This involves not only well accepted chemical and biological USP and EP testing,

conventional mechanical testing, but also biological tests using model cell lines.

Taking risk mitigation now to the next level, besides appropriate operator training, you also might consider using tools that allow assessment of correct bioreactor bag unpacking, installation and assembly with other bags, including for medium, feed and inoculum transfer. "We have therefore developed a post-installation pre-use testing approach for the entire single-use bioreactor system (including tubing) capable of detecting typical leaks that might have been introduced due to operator handling errors", says Christel Fenge. This bag testing approach is based on pressure decay, well known from testing stainless steel bioreactor assemblies using the Sartocheck®4 plus Bag tester together with a patented fleece to prevent masking of potential defects. "It has been qualified to provide a reliable test method to our single-use bioreactor bag users helping them to manage their commercial risk exposure in single-use production facilities."

The two-day conference opened with a talk by Eric Langer from BioPlan Associates, who presented his industry review of single-use systems applications, technology and 10-year trends. Thorsten Peuker from Sartorius Stedim Biotech GmbH supported the idea that we need flexible biomanufacturing processes to better address the needs of the future and cited Process4Success by way of example. On the first day, further topics included, in parallel sessions, vaccines and cell therapeutics, new developments and trends in up-streaming, down-streaming, formulation and filling, microbial and plant cell-based processes as well as PAT and single-use. The second day was dedicated to specific workshops with the main theme on SUT in biopharmaceutical manufacturing today and tomorrow. A lively debate developed during the podium discussion on the topic of 'SUT plastics: risks and acceptance'. The exhibition and poster session were very well attended, and at the end of the conference everybody enjoyed the sociable dinner and took the opportunity to exchange ideas and for networking.

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Insight into the Single-Use Production.
(Photo Sartorius)



Impressions of the BioTech2013 conference on Single-Use Technology in Biopharmaceutical Manufacturing at the ZHAW Wädenswil in June 2013. (Photo Elsbeth Heinzelmann)

**Interview with Prof. Dr. Ing. Regine Eibl
Head of Section for Cell Cultivation Technique, ZHAW
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The husband and wife professorial team of *Regine and Dieter Eibl* have set up a centre of excellence for single-user technologies at the ZHAW in Wädenswil. In 2011 they published a textbook on 'Single-Use Technology in Biopharmaceutical Manufacture' and launched the 'Single-Use Technology' network.

Professor Regine Eibl, the plastics currently restrict the application of single-use systems in upstream processing. Are there any solutions?

Although it is true that restrictions still exist in upstream processing, this is not really seen as a problem because the cell line product titres are higher now than they were a few years ago and adequate for numerous applications in 1 or 2 cubic metre bioreactors. That's why single-use systems, and in particular single-use bioreactors, have now become well established in upstream processing.

Where are the limitations in downstream processing?

The main bottleneck in downstream processing is chromatography, but this obstacle can be overcome by using multiple purification cycles or membrane adsorbers and monoliths.

Critics of single-use technology complain that the sensor technology and process analytics are not suitable for biopharmaceutical production with animal cells. Is this actually the case?

Although both continue to be weaknesses of single-use systems, there have been new developments in recent years too. One example is the BaychromAT® bioplatfrom for upstream processes in cell cultivation developed by Bayer Technology, which is a PAT (Process Analytical Technology) system with integrated data management. Specific configurations that are adapted to particular needs facilitate the fully automatic control of fermentation processes on the basis of various parameters, a solution that is particularly suitable for benchtop bioreactors.

Up to now, the major weakness of all process steps and single-use systems has been the lack of standardization and comparability, including comparability with traditional devices. How do things stand now?

Systems can now be compared to some extent. In the case of bioreactors, this is partly due to the activities of the 'Single use technology' Temporary Working Group at DECHEMA. This group has drawn up and published recommendations for characterizing single-use bioreactors. However, the problem of standardization still has to be solved, and this is an area where users need to exert greater pressure on suppliers.

The interview was conducted by Elsbeth Heinzelmänn

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