Fully disposable clinical manufacturing expands Boehringer Ingelheim's current approaches in flexible clinical supply

The bioprocessing industry in clinical production of active-pharmaceutical-ingredients (API) is facing many challenges triggered by the high demands on flexibility, productivity and cost-efficiency.

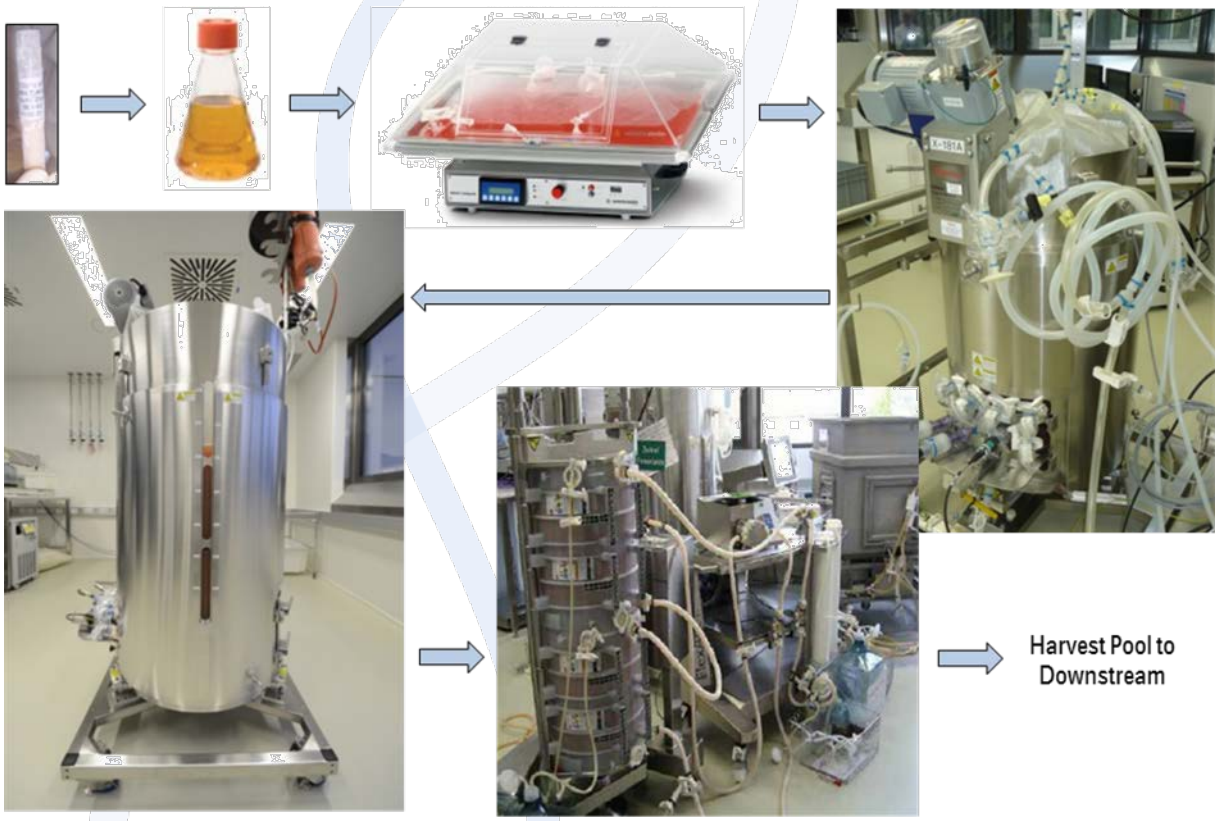
Boehringer Ingelheim offers a flexible set-up and operational approach of processing technologies within its global biopharmaceutical development network to meet these demands.

In addition to the traditional or hybrid clinical processing, the full disposable strategy enables Boehringer Ingelheim to adapt to almost any customer process and product quantity need for rapid clinical drug substance supply. Boehringer Ingelheim's long experience in clinical scale processing of various products guarantees that the customer benefits from the high expertise in efficient process transfer and process realization at comparative cost.

Before implementation of the disposable strategy various disposable process equipment suppliers were systematically screened. A large set of process equipment was thoroughly tested with respect to processing robustness and capability, GMP-compliance as well as delivery and global support reliability. The result is a unique and flexible single use platform for upstream- and downstream processing. The disposable platform is established globally in Boehringer Ingelheim's mammalian facilities and supports clients globally with the same technology as well as quality standards under GMP (good manufacturing practice). It significantly eases seamless process transfers, smooth outsourcing concepts and further boosts our new and highly flexible Lean-to-Clinic program from gene to drug product in 16 months.

The full disposable upstream process starts in shake flask and bag bioreactor systems on rocking platforms. A standard seed train with 5 passages (15 days in culture) expands the cell culture from

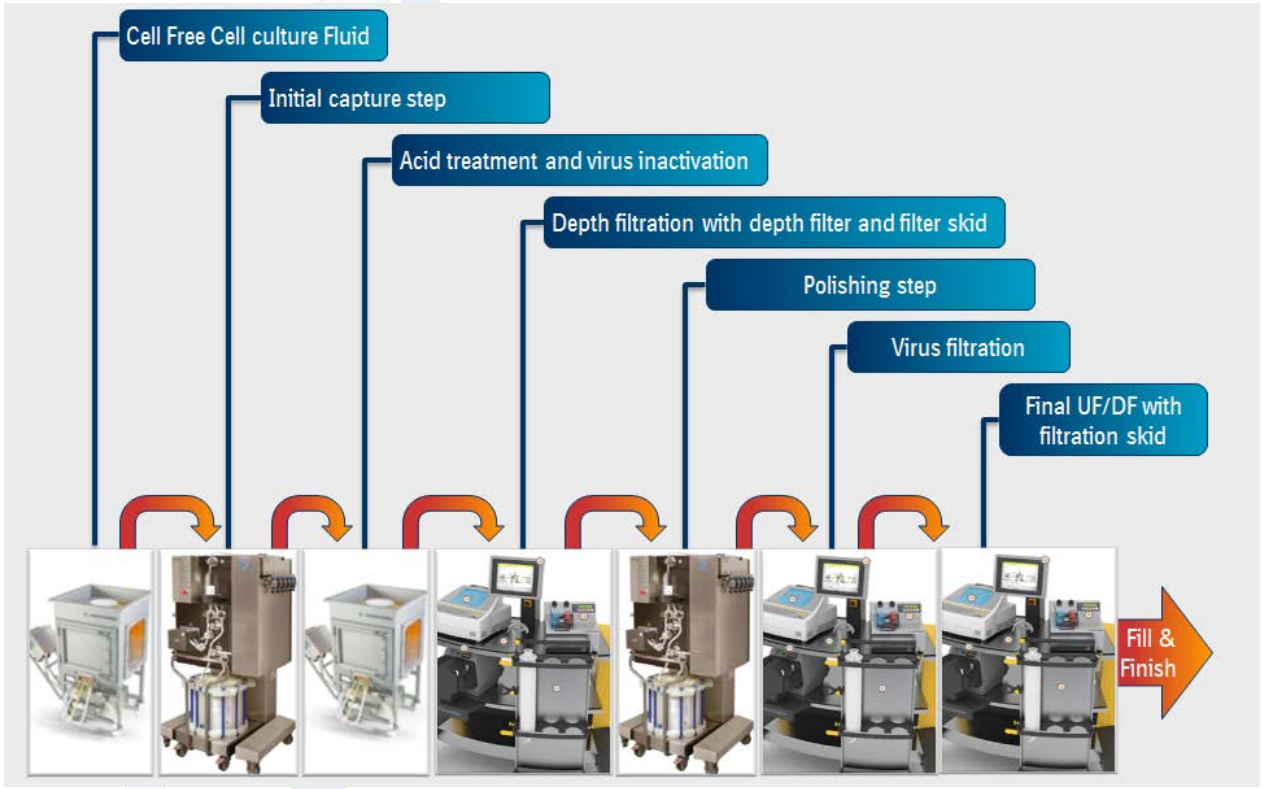
cell bank vial stage to inoculation of the 100 L single use bioreactor. Product for clinical studies can be generated at the 100 L or 500 L scale. The favored process format for the production stage is a fed batch mode with 11 or 14 days run time. Other formats and run times are feasible as well.



Boehringer Ingelheim is implementing a universal controller system that will enable the use of various single use bioreactor systems (SUBs), such as HyClone, Xcellerex, Sartorius, Millipore, ATMI. Currently, 500 L SUBs from HyClone and Xcellerex have been qualified and used for GMP manufacturing. 100 L and 500 L SUBs will be run as a global platform at Boehringer Ingelheim's sites in Biberach (Germany), Fremont (U.S.A.) and Shanghai (China).

The cell culture harvest is done by dead-end filtration. Full disposable filter elements and manifolds are used to separate the product-containing culture fluid from cells, cell debris and particles. The harvest pool is collected in a bag and handed over to downstream processing.

The filtered harvest enters the downstream in which the therapeutic protein is purified in multiple process steps. Hereby all separation techniques such as chromatography methods (e.g. affinity-ion-, hydrophobic- chromatography), tangential flow filtration and charged filters are used in full disposable mode. The special set-up enables us to transfer almost any process to full disposable processing.



Especially when processing high potent APIs the full disposable upstream and downstream processing reveals its major benefits in a multi-product facility. Hereby the utilized materials are disposed after a processing run or used product dedicated. A change over to the next campaign of a different product is significantly facilitated and safe. 'Cleaning in Place' and 'Sanitation in Place' procedures are not needed and extensive cross contamination analytics can be neglected.

The increased use of single use equipment in the past years has directed a special attention on potential leachables that may enter the product during the production process. Boehringer Ingelheim has thoroughly assessed the extractable & leachable (E&L) risk and has implemented a state of the art approach maintaining a close communication with the authorities.

If you are interested in using Boehringer Ingelheim's services in disposable clinical manufacturing, our key account managers within the Boehringer Ingelheim BioXcellence™ contract manufacturing business are happy to supply you with further information and support.

General contact: bioxcellence@boehringer-ingelheim.com

Contact Americas: bioxcellence.americas@boehringer-ingelheim.com

Contact Europe: bioxcellence.europe@boehringer-ingelheim.com

Contact Asia/Pacific: bioxcellence.asia@boehringer-ingelheim.com

Explore our website www.bioxcellence.com