

V. SIMPULAN DAN SARAN

A. Simpulan

Berdasarkan penelitian yang telah dilakukan, dapat ditarik kesimpulan bahwa.

1. Desain proses produksi produk *drug substance* dan *drug product* antibodi monoklonal terdiri atas 3 proses utama yakni proses hulu, proses hilir serta *fill and finish* dan 1 proses tambahan yakni *cell line development*. Proses hulu terbagi menjadi 4 tahapan yakni penyiapan WCB, ekspansi kultur sel, *seed training* dan produksi sedangkan proses hilir terbagi menjadi 9 tahapan yakni pemanenan sel, klarifikasi, kromatografi afinitas protein A, inaktivasi virus (metode pH rendah), kromatografi penukar kation, kromatografi penukar anion, filtrasi virus, UF/DF dan *final filtration*. Proses *fill and finish* sendiri terbagi menjadi 8 tahapan yakni *final mixing*, filtrasi steril, *aseptic filling*, *stoppering*, *sealing*, inspeksi visual, *packaging* dan penyimpanan.
2. Proses pemantauan kualitas antibodi monoklonal selama proses produksi adalah *in-process control* (IPC) atau proses kontrol selama proses produksi. IPC untuk tahapan penyiapan WCB adalah viabilitas sel, identitas sel (fenotip) dan kemurnian sel. *In-process control* (IPC) untuk tahapan ekspansi sel dan *seed training* adalah viabilitas sel dan densitas sel sedangkan IPC untuk tahapan produksi adalah viabilitas sel, densitas sel dan konsentrasi protein target. IPC untuk tahapan pemanenan sel adalah kejernihan supernatan, IPC untuk tahapan kromatografi protein A adalah

captured protein, IPC untuk tahapan kromatografi penukar kation dan anion adalah *purity* dan pH bufer elusi, IPC untuk tahapan filtrasi virus adalah integrasi filter, IPC untuk proses UF/DF adalah HCP dan residu protein A dan IPC untuk proses *final filtration* adalah *filter integrity*. IPC untuk tahapan *final mixing* adalah pH, konduktivitas, warna, kejernihan dan osmolaritas, IPC untuk tahapan filtrasi steril adalah endotoksin dan *bioburden*, IPC untuk tahapan *aseptic filling* adalah *filling volume*, IPC untuk tahapan *stoppering* dan *sealing* adalah kebocoran, IPC untuk tahapan inspeksi visual adalah *particulate*, *appearance* dan *primer packaging* dan IPC untuk tahapan pengemasan adalah keadaan karton, label, tanggal kadaluwarsa, dan *information card*.

3. Pengaruh neraca massa terhadap penentuan desain proses produksi antibodi monoklonal adalah berapa banyak material yang akan digunakan (Rituximab, polisorbat 80, natrium klorida, natrium sitrat dihidrat dan WFI), berapa banyak produk yang dihasilkan, berapa banyak produk yang hilang selama proses produksi, jumlah *batch* produksi per tahun (6 *batch*), skala produksi (1.500 L) hingga ukuran instrumen produksi yang akan digunakan (ukuran bioreaktor dan kapasitas filter).
4. Tahapan proses produksi antibodi monoklonal dari tahap hulu, hilir dan *fill and finish* telah memenuhi konsep kesetimbangan massa yang didasarkan pada perhitungan teoritis jumlah aktual material masuk dan keluar serta selisih antara jumlah material yang masuk dan keluar.

B. Saran

Penelitian selanjutnya lebih baik melakukan desain proses produksi secara spesifik untuk produk antibodi monoklonal tertentu dari proses hulu hingga proses *fill and finish*. Penelitian selanjutnya juga disarankan untuk melakukan proses *trial*. Proses *trial* dilakukan guna membuktikan konsep kesetimbangan massa yang sudah dikalkulasi sebelumnya.



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