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(54) **Title**: CELL-CONTROLLED PERFUSION IN CONTINUOUS CULTURE

(57) **Abstract**: Methods of protein production in continuous perfusion mammalian cell culture bioreactors are provided. Methods for continuous perfusion culture by allowing cells to self-regulate the rate of addition of perfusion medium to the bioreactor via a pH change are presented. Compositions comprising the perfusion medium as well as the process advantages of using hi-end pH control of perfusion or HIPCOP are also presented.