

DEVELOPING A CONTROL STRATEGY FOR SEQUENCE VARIANTS

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High productivity cell culture processes are being developed at Regeneron to meet the increasing patient demand for biological products across a broad product pipeline. The cellular demands of these high productivity processes drive amino acid consumption. Amino acid substitutions or sequence variants may occur upon amino acid depletion during protein production. Sequence variants are an undesirable product quality attribute that should be minimized to ensure patients are dosed with a protein of the intended sequence. Sequence variant control strategies have been developed at Regeneron utilizing more readily measured metabolites as opposed to direct sequence variant measurement by mass spectrometry. Different control strategies exist for essential and nonessential amino acids. The control strategy has been implemented across a number of processes at Regeneron during process development reducing the frequency of sequence variant detection and ensuring protein is produced of the intended quality while achieving high productivities.