Limiting factors

- Peptides are complex molecules and each peptide sequence is unique with regard to its chemical and physical properties. These properties very often change as the synthesis proceeds. Consequently, coupling efficiency of amino acids during the synthesis and the ultimate purity of the final product is highly conditioned by the sequence. Some peptides are difficult or even impossible to synthesize.
- The longer the peptide chain, the higher the chance of aggregation, peptide truncation, purification difficulties and low yield.
- Peptides containing hydrophobic amino acids (A, W, L, I, F, M, V, and P) are more difficult to synthesize and result in reduced yield.
- Peptides with zero charge tend to be insoluble
- Methionine, tryptophan and cysteine residues are susceptible to rapid oxidation and can interfere with peptide cleavage and purification. If a cysteine or a methionine are not absolutely required, consider replacing cysteine by the hydrophobic α-aminobutyric acid or by the polar serine and methionine with norleucine.
- Peptides containing a single free thiol group may be oxidized yielding dimers. Cyclic peptides or oligomers may be obtained from peptides containing several Cys residues.
- When designing a polypeptide, try to avoid a proline residue at its C-terminus.
- Avoid placing glutamine at the N-terminal because it is unstable and will turn into cyclic pyro-glutamic acid.
- The presence of consecutive serine residues in a peptide chain may lead to lower purity and higher deletion products as a result of isomerization.
- Asp-containing peptides are susceptible to acid-catalyzed aspartimide formation. Avoid Asp-Ser, Asp-Pro and Asp-Gly pairs.