

## Allowable Adjustments to Pharmacopoeia Methods for ISOCRATIC SEPARATIONS

Component	United States Pharmacopoeia (USP)	European Pharmacopoeia (Ph. Eur.)
<b>Mobile phase minor component (<math>\leq 50\%</math>)</b>	$\pm 30\%$ Relative; Cannot exceed $\pm 10\%$ Absolute change; Cannot be reduced to zero	$\pm 30\%$ Relative or $\pm 2\%$ absolute, whichever is the larger; Cannot exceed $\pm 10\%$ Absolute change
<b>Mobile phase pH</b>	$\pm 0.2$ pH units	$\pm 0.2$ pH units; $\pm 1.0$ for non-ionizable substances
<b>Buffer concentration</b>	$\pm 10\%$	$\pm 10\%$
<b>Column temperature</b>	$\pm 10^\circ\text{C}$	$\pm 10^\circ\text{C}$
<b>Injection volume</b>	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection reqs.	Can be reduced so long as precision and detection limits are met
<b>Detector wavelength</b>	Cannot be modified	Cannot be modified
<b>Flow rate</b>	$\pm 50\%$ (at given ID)	$\pm 50\%$ (at given ID; flow rates may be adjusted more when changing inner diameter)
<b>Column inner diameter</b>	Can be adjusted so long as linear velocity is maintained	$\pm 25\%$
<b>Column length</b>	Column length (L) to particle size diameter (dp) ratio can be adjusted between $-25\%$ and $+50\%$ *	Column length may be adjusted $\pm 70\%$
<b>Particle size</b>	Column length (L) to particle size diameter (dp) ratio can be adjusted between $-25\%$ and $+50\%$ *	Particle diameter may be reduced as much as $50\%$
<b>Stationary Phase</b>	No change of the identity of the substituent permitted	No change of the identity of the substituent permitted

\*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within  $-25\%$  to  $+50\%$

## Allowable Adjustments to Pharmacopoeia Methods for GRADIENT SEPARATIONS

Component	United States Pharmacopoeia (USP)	European Pharmacopoeia (Ph. Eur.)
<b>Mobile phase minor component (<math>\leq 50\%</math>)</b>	Changes to gradient composition are not recommended	Minor adjustments of the composition of the mobile phase and the gradient are acceptable, if the system suitability requirements are met, the principle peak(s) elute(s) within $\pm 15\%$ of the indicated retention time(s) and the final elution power of the mobile phase is not weaker.
<b>Mobile phase pH</b>	$\pm 0.2$ pH units	No adjustment permitted
<b>Buffer concentration</b>	$\pm 10\%$	No adjustment permitted
<b>Column temperature</b>	$\pm 10^\circ\text{C}$	$\pm 5^\circ\text{C}$
<b>Injection volume</b>	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection reqs.	Can be reduced so long as precision and detection limits are met
<b>Detector wavelength</b>	Cannot be modified	Cannot be modified
<b>Flow rate</b>	For gradient separations, changes to flow rate are not allowed	Adjustment is permitted to maintain linear velocity when changing column dimensions
<b>Column inner diameter</b>	For gradient separations, changes to column length, particle size, or inner diameter are not allowed	$\pm 25\%$
<b>Column length</b>	For gradient separations, changes to column length, particle size, or inner diameter are not allowed	$\pm 70\%$
<b>Particle size</b>	For gradient separations, changes to column length, particle size, or inner diameter are not allowed	No change permitted
<b>Stationary Phase</b>	No change of the identity of the substituent permitted	No change of the identity of the substituent permitted