Allowable Adjustments to Pharmacopoeia Methods for

ISOCRATIC SEPARATIONS

Component	United States Pharmacopoeia (USP)	European Pharmacopoeia (Ph. Eur.)
Mobile phase minor component (≤ 50 %)	± 30 % Relative; Cannot exceed ± 10 % Absolute change; Cannot be reduced to zero	± 30 % Relative or ± 2 % absolute, whichever is the larger; Cannot exceed ± 10 % Absolute change
Mobile phase pH	± 0.2 pH units	± 0.2 pH units; ± 1.0 for non-ionizable substances
Buffer concentration	± 10 %	± 10 %
Column temperature	± 10 °C	± 10 °C
Injection volume	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
Detector wavelength	Cannot be modified	Cannot be modified
Flow rate	± 50% (at given ID)	± 50 % (at given ID; flow rates may be adjusted more when changing inner diameter)
Column inner diameter	Can be adjusted so long as linear velocity is maintained	± 25 %
Column length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	Column length may be adjusted ± 70 %
Particle size	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 %
Stationary Phase	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.)
Mobile phase minor component (≤ 50 %)	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 ± 15 % of the indicated retention time(s) and the final elution power of the mobile phase is not weaker.
Mobile phase pH	± 0.2 pH units	No adjustment permitted
Buffer concentration	± 10 %	No adjustment permitted
Column temperature	± 10 °C	± 5 °C
Injection volume	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
Detector wavelength	Cannot be modified	Cannot be modified
Flow rate	For gradient separations, changes to flow rate are not allowed	Adjustment is permitted to maintain linear velocity when changing column dimensions
Column inner diameter	For gradient separations, changes to column length, particle size, or inner diameter are not allowed	± 25 %
Column length	For gradient separations, changes to column length, particle size, or inner diameter are not allowed	± 70 %
Particle size	For gradient separations, changes to column length, particle size, or inner diameter are not allowed	No change permitted
Stationary Phase	No change of the identity of the substituent permitted	No change of the identity of the substituent permitted