

## Guidance Number: 019

### Appendix I. Recommended Acceptance Criteria for Quantitative Tests

Number of reference batches	Distribution of data	Recommended Acceptance Criterion for Quantitative Tests: Results should fall...
At least 10	Normal (Gaussian)	within mean +/- 3 standard deviations (SD), if confident reference data represents process capability, or within historical range and release limits
At least 10	Non-Gaussian	within release limit and historical range. Consider if data indicate process inconsistency.
Less than 10	Normal or non-Gaussian	within release limit

Historical range = maximum and (if appropriate) minimum for reference batches.

**Appendix II. Example of statistical analysis of impurity and purity data for equivalence evaluation**

This table shows historical HPLC purity and impurities and residual solvents data. Note that lot 1008 was rejected and therefore omitted from the table. See also explanatory notes below and on next page.

API Impurity Profile (HPLC method xxx)							Residual solvents (GC method yyy)	
ID →	Impurity A	Impurity B	Impurity C		Impurity D	Total Imps	THF	Methylene chloride
RRT →	0.35	0.67	1.31	1.76	2.67			
Release limit	NMT 0.5%	NMT 0.3%	NMT 0.2%	NMT 0.1%	NMT 0.3%	NMT 1.0%	NMT 0.5%	NMT 600 ppm
Historical batches								
1001	0.06	0.08	BQL	0.13	0.15	0.59	0.20	310
1002	0.07	0.07	BQL	0.05	0.22	0.54	0.22	244
1003	0.08	0.07	BQL	0.12	0.15	0.62	0.18	LT 200
1004	0.10	0.11	BQL	0.10	0.08	0.63	0.17	379
1005	0.15	0.27	BQL	BQL	0.12	0.84	0.18	217
1006	0.40	0.12	BQL	0.07	0.08	0.75	0.19	LT 200
1007	0.15	0.10	BQL	BQL	0.07	0.42	0.16	LT 200
1009	0.22	0.18	BQL	BQL	0.07	0.61	0.19	286
1010	0.15	0.08	BQL	BQL	0.08	0.42	0.21	211
1011	0.08	0.12	BQL	BQL	0.05	0.59	0.20	LT 35
Mean	0.146	0.120	BQL	0.047	0.107	0.601	0.190	164.7
SD	0.102	0.062	--	0.054	0.053	0.129	0.018	149.6
Mean+3SD	0.45	0.31	--	0.21	0.26	0.99	0.24	613.5
Mean-3SD	--	--	--	--	--	--	--	--
Equivalence acceptance criterion	NMT 0.4% **	NMT 0.3% **	NMT 0.2% ***	NMT 0.1% #	NMT 0.3% ***	NMT 1.0% *	NMT 0.3% ##	NMT 600 #

NMT = not more than; LT = less than; NLT = not less than; BQL = beneath quantitation limit (or none detected); RRT = relative retention time.

\* = Acceptance criterion is the mean +/- 3 SD value determined from above historical data.

\*\* = Acceptance criterion is historical maximum (or minimum) value. For Impurities A and B, one historic result is significantly different than the others, distorting the mean + 3 SD calculations, so the maximum values are suggested as equivalence criteria. (Max., mean + 3 SD, and release limit are the same for Impurity B.)