Change the following as follows:

System Suitability 〈*G1-2-181*〉

In order to ensure the reliability on the results of drug analyses, it is essential to verify that the test method to be applied to the test, including the method prescribed in the Japanese Pharmacopoeia (JP), can give the results adequate for its intended use using the analytical system in the laboratory in which the test is to be performed, then to carry out system suitability testing for confirming that the analytical system maintains the state suitable for the quality test.

1. Definition and role of system suitability

''System Suitability'' is the concept for ensuring that the performance of the analytical system is as suitable for the analysis of the drug as was at the time when the verification of the test method was performed using the system. Usually, system suitability testing should be carried out at every series of drug analysis. The test procedures and acceptance criteria of system suitability testing must be prescribed in the test methods of drugs. The results of drug analyses are not acceptable unless the requirements of system suitability have been met.

System suitability testing is an integral part of test methods using analytical instruments, and based on the concept that the equipments, electronic data processing systems, analytical operations, samples to be analyzed and operators constitute an integral system that can be evaluated, when the test procedures and acceptance criteria of system suitability testing are prescribed in the test methods.

2. Points to consider in setting system suitability

Parameters of system suitability testing to be prescribed in the test method depend on the intended use and type of analytical method. Since system suitability testing is to be carried out in a routine manner, it is preferable to select the parameters necessary for ensuring that the analytical system maintains the state suitable for the analysis of the drug and to prescribe its test procedure able to carry out easily and rapidly.

For example, in the case of quantitative purity tests using liquid chromatography or gas chromatography, the evaluation of parameters such as ''System performance'' (to confirm the ability to analyze target substance specifically), ''System repeatability'' (to confirm that the degree of variation in the analytical results of target substance in replicate injections is within the allowable limit) and ''Test for required detectability'' (to confirm the linearity of chromatographic response around the specification limit) are usually required.

The specifications of system suitability in chromatography should be in accordance with Chromatography <*2.00*> or Liquid Chromatography <*2.01*>.

The followings are supplements to the section of system suitability prescribed in ''Liquid Chromatography <*2.01*> ''.

2.1. System repeatability of HPLC and GC

2.1.1. Allowable limit of system repeatability

It is described in the section of system suitability in ''Liquid Chromatography <*2.01*>'' that ''In principle, total number of replicate injections should be 6'', and ''The allowable limit of ''System repeatability'' should be set at an appropriate level based on the data when suitability of the method for the evaluation of quality of the drug was verified, and the precision necessary for the quality test''.

Based on the above description, an allowable limit of system repeatability for 6 replicate injections should be set in consideration with the following descriptions. However, in the case that the test method prescribed in the JP monograph is used for the test, the allowable limit of system repeatability prescribed in the monograph should be applied.

(i) Assay for drug substance (for drug substance with the content nearby 100%): An adequate allowable limit should be set at the level that the chromatographic system is able to give the precision suitable for the evaluation of variation in the content of active ingredient within and among the batches of drug substance. For example, the allowable limit of ''not more than 1.0%'' is usually recommended for the drug substances whose width of content specification are not more than 5%, as is in the case of content specification of 98.0 – 102.0% which is often observed in the assay using liquid chromatography.

(ii) Assay for drug products: An adequate allowable limit should be set considering the width of content specification of the drug product and the allowable limit prescribed in the assay of drug substance (when the drug product is analyzed by a method with the same chromatographic conditions as those used for the analysis of drug substance).

(iii) Purity test for related substances: An adequate allowable limit should be set considering the concentration of active ingredients in the solution used for the system suitability testing. In the case that a solution with active ingredient concentration of 0.5 – 1.0% is used for the test of system repeatability, an allowable limit of ''not more than 2.0%'' is usually recommended.

Recommendations for allowable limits described above should not be applicable to gas chromatography.

2.1.2. Method for decreasing the number of replicate injections without losing the quality of system repeatability testing

It is described in the section of system suitability in ''Liquid Chromatography <*2.01*>'' that ''In principle, total number of replicate injections should be 6. However, in the case that a long time is necessary for one analysis, such as the analysis using the gradient method, or the analysis of samples containing late eluting components, it may be acceptable to decrease the number of replicate injections by adopting new allowable limit of ''System repeatability'' which can guarantee a level of ''System repeatability'' equivalent to that at 6 replicate injections.''

In consideration of the above description, a method for decreasing the number of replicate injections without losing the quality of system repeatability testing is shown below. By utilizing this method, if necessary, one can set the test for system repeatability with reduced number of replicate injections and also change the test setting once being set. In addition, the latest Ministerial Ordinance on Good Manufacturing Practice, related notifications and administrative notices

should be referred to for the pharmaceutical affairs procedures for changing the number of replicate injections.

The following table shows the allowable limits to be attained in the test at 3 – 5 replicate injections (n = 3 – 5) to keep the quality test equivalent to that of test at n = 6.

However, it should be kept in mind that decrease in the number of replicate injections results in increase in the weight of each injection, it becomes more important to maintain the equipment in a suitable state.

Table Allowable limits to be attained in the test at 3 - 5 replicate injections (n = 3 – 5) to keep the quality of test equivalent to that of test at n = 6*

		Allowable limit (RSD)					
Allowable limit prescribed in the test of n = 6		1%	2%	3%	4%	5%	10%
Allowable limit to be attained	n = 5	0.88%	1.76%	2.64%	3.52%	4.40%	8.81%
	n = 4	0.72%	1.43%	2.15%	2.86%	3.58%	7.16%
	n = 3	0.47%	0.95%	1.42%	1.89%	2.37%	4.73%

* The probability for inadequate analytical systems to meet the requirements of system suitability testing, is supposed to be 5%.