Annex 1

Certification Criteria for *In Vitro* Diagnostics

For the *in vitro* diagnostics specified in the Announcement issued in 2005 for which the criteria were enacted by the Minister of Health, Labour and Welfare in accordance with the provision in Article 23-2-23, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices, the details on application of the criteria in the Announcement are hereby established as follows (See the annex table for the *in vitro* diagnostics subject to these criteria).

Certification criteria for *in vitro* diagnostics

1. Qualitative Reagents
   Concerning qualitative reagents, the concordance rate shall be 90% or more, which is calculated by the statistical processing indicated in Attachment 3, when compared with the control *in vitro* diagnostics or detecting methods that meet the conditions indicated in Attachment 2 using the test method indicated in Attachment 1.

2. Quantitative Reagents
   Concerning quantitative reagents, the correlation coefficient shall be 0.9 or more and the slope of the regression equation shall be in a range of 0.9 to 1.1, which are calculated by the statistical processing of the measured results as indicated in Attachment 3, when compared with the control *in vitro* diagnostics or measuring methods that meet the conditions indicated in Attachment 2 using the test method indicated in Attachment 1.

3. Conformity to the Essential Principles
   Conformity to the Essential Principles shall be demonstrated on the basis of the Essential Principles Checklist indicated in the Checklist Notification.

4. Others
   These criteria do not apply to *in vitro* diagnostics that are clearly different from existing *in vitro* diagnostics in measurement principles, detective sensitivity, etc., even if they meet these criteria.

Attachment 1

Test method

1) Person(s) who conduct the test

The test shall be conducted by the applicant(s) themselves or other testing laboratories at the applicants' request. Statements and signatures of the person(s) who conducted the test shall be provided in the test result documents.

2) Number and selection method of the specimens

[1] Number of specimens

Shall be 50 or more in principle, and the specimens shall be appropriately sampled by the usual method and appropriately stored. However, this does not necessarily apply in case the performance can be properly evaluated or if the number of patients with the target disease is extremely small.

[2] Qualitative Reagents

In principle, the number of specimens in the smaller of the positive and the negative groups shall be 25 or more, and the specimens shall be selected to evaluate the performance properly by including those near the clinical decision concentration (cutoff value, etc.). However, this does not necessarily apply in case the number of patients with the target disease or the number of specimen types concerning the target disease is extremely small, or it is difficult to confirm the specimens near the clinical decision concentration.

[3] Quantitative Reagents

The concentration of specimens shall be distributed over the entire measurement range, and the specimens near the clinical decision concentration (reference value, cutoff value, etc.) shall be included so that the performance can be properly evaluated. However, this does not necessarily apply in case the number of patients with the target disease or the number of specimen types concerning the target disease is extremely small.

Attachment 2

Control *in vitro* diagnostics, or detecting or measuring methods

As control *in vitro* diagnostics, *in vitro* diagnostics that are widely used in the actual clinical setting and of which the performance, such as reproducibility, is excellent in view of the current technological level, shall be selected among previously approved or certified ones.

If there are multiple previously approved (or certified) *in vitro* diagnostics to be listed as control candidates, at least two types of *in vitro* diagnostics shall be selected as control *in vitro* diagnostics. In addition, if there are multiple measuring methods, at least two types of *in vitro* diagnostics shall be selected as controls so that measurement can be conducted with multiple methods. Concerning quantitative reagents, when the Y intercept of the regression line derived from measured data of an *in vitro* diagnostics to be tested and a control candidate is far from the origin, it is recommended not to select the candidate *in vitro* diagnostics as a control.

Meanwhile, if there is a standard detecting or measuring method which is adopted by public organizations (e.g., WHO), standards developing organizations (e.g., JCTLM, CLSI, and JCCLS), related academic societies, etc., data obtained by this detecting or measuring method shall be principally employed as the control data. In this case, the relevant scientific explanation of the adequacy for the standard method shall be provided although the standard method is adopted by academic societies, etc. (The term “standard method” as used herein refers to a method recognized as a standard method in the world or Japan. In this case, the procedural methods, criteria, performance standards, etc. specified in the standard methods shall be explained.)

(Note)
JCTLM: Joint Committee on Traceability in Laboratory Medicine
CLSI: Clinical and Laboratory Standards Institute
JCCLS: Japanese Committee for Clinical Laboratory Standards

Attachment 3

Methods of statistical processing

The following statistical processing shall be conducted for detected or measured results of control *in vitro* diagnostics, or detecting or measuring method(s).

(1) Qualitative Reagents

The detected results of identical specimens for control product(s) and a test product shall be shown in adequate table form (an m x n matrix, for example), and the concordance rate shall be calculated.

(2) Quantitative Reagents

The measured values (X, Y) for the identical specimens shall be depicted as a plot of the measured results of a test product on the Y-axis and those of the control product on the X-axis, and the correlation coefficient and linear regression equation of the measured values shall be determined.