Annex 1

Approval Criteria for *In Vitro* Diagnostics

For *in vitro* diagnostics specified in the annex table (Class III *in vitro* diagnostics excluding *in vitro* diagnostics for genetic testing of HIV, HCV, HDV, HTLV, and other pathogens, and human genetic testing), the approval criteria are hereby established as follows.

Approval 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 100 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 50 or more, and the specimens shall be selected 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.

In addition, this method shall apply to semi-quantitative reagents and identification reagents for bacteria.

[3] Quantitative Reagents

The concentration of specimens shall be distributed over the entire measurement range, and specimens near the clinical decision concentration (reference value, cutoff value, etc.) shall be included in the selection. 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. It shall not be allowed to select qualitative reagents (semi-quantitative reagents) with indicated values that are not in a range corresponding to that of the reagent to be tested, as controls. Concerning quantitative reagents, when the Y intercept of the regression line derived from measured data of an *in vitro* diagnostic 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.