Guidelines for Registration of In Vitro Diagnostic Medical Device

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A. Introduction

The Registration of In Vitro Diagnostic Medical Device (IVD) shall be done according to Guidelines for Registration of Medical Devices and relevant regulations. In the present guidance, In vitro diagnostic medical device (IVD) are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. While "In Vitro Diagnostic Reagents" are referring to reagent, calibrator or control material for the above described purpose.

To facilitate an effective regulatory control of IVD, ensuring the safety and effectiveness of such products, the present guidance by Ministry of Health and Welfare (MOHW) aims to provide supplementary information on registration of class II and class III IVD. The following documents shall be submitted to demonstrate the safety and effectiveness of the device, when applying for the registration and market approval of class II and class III IVD, as according to Article 15 and 17 of Guidelines for Registration of Medical Devices:

I. Chinese translation of instructions, manual, packaging, and labels shall be affixed or stapled to the label attachment form.

II. The pre-clinical testing and original manufacturer quality control test specifications and methods, original test records, and test report.

III. Information on product construction, materials, specifications,

performance, uses, and drawings etc. However, in the case of instruments, operating manuals and service handbooks covering the items in this subparagraph may be submitted instead.

IV. Theoretical basis and relevant research reports and data.

V. Clinical trial reports.

VI. Radiation safety information for equipment emitting ionizing radiation.

B. Scope

The scope of the present document is confined to the devices described in Annex I of the Regulations Governing Management of Medical Devices promulgated by the Ministry of Health and Welfare (the Ministry), as indicated in Attachment 1:

A CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES;

B HEMATOLOGY AND PATHOLOGY DEVICES, and;

C IMMUNOLOGY AND MICROBIOLOGY DEVICES.

C. Application Information for Registration of Class II In Vitro Diagnostic Medical Device (administrative information not included)

Article 1 Chinese translation of instructions, manual, packaging, and labels shall contain the following information:

I. Photographs or product brochure describing the device.

II. Package Inserts in Chinese or package inserts in foreign language with a corresponding Chinese translation. Each device shall be accompanied by the appropriate information, taking account of the training and knowledge of the potential users, by attaching or affixing the information onto the sales packaging.

III. Where appropriate, symbol and identification color used shall conform to the international harmonized standards (e.g. EN 980, ISO 15223) or the relevant announcement made by Ministry of Health and Welfare (MOHW). If no relevant standards exist, the manufacturer shall provide a clear description and explanation about the symbols and color used with the product.

IV. In the case of IVD which may be considered as being dangerous, taking account of the nature and quantity of its constituents and the form under which they are present, labeling requirements according to relevant announcement made by MOHW shall be followed. If there is insufficient space to put all the information on the device itself or on its label, the relevant warning symbols shall be put on the label or instructions for use.

V. The labeling and packaging shall contain relevant information with reference to Appendix

Article 2 Information on the pre-clinical testing and original manufacturer quality control test specifications and methods, original test records, and test results report, taking into account the nature and properties of the IVD, shall contain the following:

I. Basic information shall in general include, but not limited to the following:

(I) Sensitivity;

(II) Specificity;

(III) Interference study;

(IV) Accuracy;

(V) Precision/Reproducibility;

(VI) Validation of cut-off value;

(VII) Stability;

(VIII) Traceability;

(IX) Other chemical, physical, electrical, mechanical, biological, electrical safety, electromagnetic compatibility, software validation, sterility or microbiological control information relevant for demonstrating compliance to the safety and effectiveness requirement

(X) A representation and description of the manufacturing process flow.

(XI) A description of test methods specification, and Certificate of Analysis for the active ingredient(s), raw materials derived from human and animals and the final product should be provided.

II. Pre-clinical performance evaluation may be carried out in direct comparison with a device, which is currently marketed in Taiwan or one of the following countries or areas: United States, Japan, Canada, Switzerland, Australia, or European Union. If there is no similar product available for comparison testing, the following alternatives can be used in order:

(I) Conduct the comparison testing with the reference method.

(II) Comply with the recognized standards or other international standards

(III) Use a widely accepted industrial testing method.

III. Information on pre-clinical testing shall include:

(I) the description of study design, including but not limited to e.g. materials used, method, acceptance criteria etc.

(II) the method of data analysis.

(III) the study report (can be graphically presented).

(IV) the study conclusion.

(V) Review of the registration will be based on submitted documents containing the above described information, and when necessary, raw data of tests shall be submitted upon request.

IV. User performance evaluation/usability study for home-use IVD device, if appropriate, shall be conducted to determine the device's performance when used by lay users, unassisted, following instructions provided in the labeling.

V. Documentation on sterilization process validation shall be submitted for sterile product.

VI. The operating instructions for devices emitting radiation giving detailed information as to the nature of the emitted radiation, means of protecting the user, and on ways of avoiding misuse and of eliminating the risks inherent in installation.

VII. For IVDs of new testing items, new methods, new theories, or new clinical applications that do not have similar products, theoretical bases and relevant research reports should be submitted along with clinical evaluation reports in addition to the above materials. The clinical evaluation may be conducted in accordance with Article 13 of Chapter 4.

Article 3 Submission of product construction, materials, specifications, performance, uses, and drawings information. In the case of instruments, operating manuals and service handbooks covering the items in this Subparagraph may be submitted instead.

I. The intended use. This may include:

(I) what is being detected by the assay;

(II) whether the assay is automated;

(III) what the device is intended for;

(IV) whether the test is qualitative, quantitative or semi-quantitative;

(V) for a specific disorder, condition or risk factor of interest that the test is

intended to detect, define or differentiate;

(VI) the type of specimen(s) required (eg. serum, plasma, whole blood, tissue biopsy, urine);

(VII) testing population.

II. A clear statement of the function of the IVD medical device (screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease);

III. A general description of the principle of the assay method or instrument principles of operation;

IV. The intended user (lay person or professional);

V. A description of all components of the assay, including but not limited to antibodies, antigens, nucleic acid primers, buffers, assay controls and calibrators used with the IVD medical device;

VI. A description of the specimen collection and transport materials provided with the IVD medical device;

VII. A description of the appropriate assay characteristics or dedicated assays for instruments of automated assays;

VIII. A description of the appropriate instrumentation characteristics or dedicated instrumentation for automated assays;

IX. A description of any software to be used with the IVD medical device;

X. A description or complete list of the various configurations/variants of the IVD medical device that will be made available;

XI. If applicable, a description of the accessories, other IVD medical device and other products which are not IVD medical device, and are intended to be used in combination with the IVD medical device.

D. Special Requirements for Class III In Vitro Diagnostic Medical Device

Article 4 For Class III IVD, in addition to the information mentioned in Chapter III, the following supplementary information shall be submitted:

I. Specification and analytical methods of active ingredient and semi-finished product. (if appropriate)

II. Specification and technical information of final product.

III. The manufacturing and purification process of final product. (if appropriate)

IV. Process Control or Batch Production Records

V. Stability information (if appropriate)

VI. Analytical Method Validation documents

VII. Clinical Evaluation Reports

Article 5 Specification and analytical methods of main active ingredient and semi-finished product:

I. Original manufacturer's specification of main active ingredient and semi-finished product shall be submitted:

(I) Characterization and Description: A clear description of each main active ingredient and semi-finished product shall be provided. These descriptions may include, but are not limited to, any of the following: chemical structure, primary and subunit structure, molecular weight, molecular formula, name, antibody class/subclass, etc., as appropriate. Results of all characterization analytical testing shall be submitted, including information on identity, potency, specificity, purity, stability, consistency, etc.

(II) Physicochemical Characterization: the following list of analysis should be performed as necessary:

1.

(1) amino acid analysis

(2) amino- and carboxyl-terminal sequencing
(3) full amino acid sequencing
(4) nucleic acid sequencing
(5) peptide mapping/enzymatic mapping
(6) determination of disulfide linkage
(7) Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis (SDS-PAGE) (reduced and non-reduced)
(8) isoelectric focusing
(9) Conventional and High Pressure Liquid Chromatography (HPLC), e.g., reverse-phase, size exclusion, ion-exchange, etc.
(10) mass spectroscopy
(11) assays to detect substance-related proteins including deaminated, oxidized, clipped, and aggregated forms and other variants, e.g., amino acid substitutions, adducts/derivatives
(12) assays to detect residual non-specific host proteins, DNA, reagents
(13) immunochemical analyses
(14) assays to quantitate bioburden and endotoxin
(15) antibody neutralization
(16) hemagglutination
(17) hemagglutination inhibition
(18) protein nitrogen level

2. Additional physicochemical characterization may be necessary for substances undergoing post-translational modifications, e.g., glycosylation, and for substances derivatized with other agents, including other proteins, enzymes, radionuclides, or chemicals. The information submitted shall include the degree of derivatization or conjugation, the amount of unmodified substance, removal of free materials (e.g., enzymes, proteins radionuclides, etc.), and the stability of the modified substance as a result of the

manufacturing process.

3. All test methods shall be fully described, and the results provided. The application shall also include the actual data such as chromatograms, photographs of SDS-PAGE or agarose gel, spectra, etc.

4. Information of the above shall be submitted with acceptance criteria, testing procedures and testing results to facilitate submission review.

(III) SPECIFICATIONS/ANALYTICAL METHODS

1. Specifications and Tests for main active ingredients and semi-finished products:

Specifications and analytical methods used for release testing, shelf life determination and distribution conditions shall be described in detail, in addition to the specifications and tests for their identity, purity, strength and/or potency, specificity, and batch to batch consistency. The analytical systems shall be validated and the data shall be provided for non-compendial methods to demonstrate the system suitability.

2. Impurities Profile

If appropriate, analytical information of variants of the protein main active ingredient and semi-finished product (e.g., clipped, aggregated, deaminated, and oxidized forms), as well as non-product related impurities (e.g., process reagents and cell culture components), shall be included.

II. REFERENCE STANDARDS/PANELS

(I) Reference Standard: If an International Reference Standard is used, the citation for the standard and a certificate of analysis shall be submitted. If no reference standard exists and the applicant establishes in-house, primary reference standards, a description of the characterization, specifications and test report of the standards shall be provided.

(II) In-house Reference Standard: In-house working reference standards shall

be used and the descriptions of the preparation, characterization, specifications, testing, substitutions, and results shall be provided.

Article 6 The Specification of the finished product

In addition to the information mentioned in Article 2, the original manufacturer quality control test specifications and methods, original test records, and test results report, a description of the finished product including the composition, such as quantity, ratio or formulation etc shall be submitted. The test report shall include:

I. The lot/batch number, test date, signatures of the tester and the responsible person.

II. Test reports of main active ingredient used, semi-finished product and finished product.

III. Test results against each and all specification.

IV. Test reports for the main active ingredient of the batch that is being used to manufacture the specified finished product.

V. Test data for quantitative test result, and “Pass” or “Fail” for presenting result of comparison test against standard reference materials

Article 7 COMMON TECHNICAL SPECIFICATIONS (CTS)

CTS for IVD in the detection, confirmation and quantification of markers of HIV infection (HIV 1 and 2), HTLV I and II, and hepatitis (HAV, HBV, HCV, HDV, HEV) should include the following:

I. Devices which detect virus infections placed on the market for use as either screening or diagnostic tests, shall meet the same requirements for sensitivity and specificity.

II. Devices intended for testing body fluids other than serum or plasma, e.g. urine, saliva, etc. shall meet the same CTS requirements for sensitivity and specificity as serum or plasma tests. The clinical performance evaluation shall test samples from the same individuals in both the tests to be approved

and in a respective serum or plasma assay.

III. Devices intended for self-test, shall meet the same CTS requirements for sensitivity and specificity as respective devices for professional use. Relevant parts of the performance evaluation or usability study shall be carried out (or repeated) by appropriate lay users to validate the operation of the device and interpretation of test result.

IV. Devices intended for early stage infection (seroconversion), the sensitivity shall be evaluated with sero-conversion panels.

V. Negative specimens intended for used in a clinical performance evaluation shall be able to reflect the target population for which the test is intended, for example blood donors, hospitalized patients, pregnant women etc.

VI. Devices intended for screening of blood donor, the donor population profile of at least two blood donation centers shall be studies before performing the performance evaluations.

VII. Devices intended to screen for blood donors shall have a specificity of at least 99.5%, justification shall be provided for any discrepancy.

VIII. Devices intended to be used with serum and plasma, the performance evaluation shall demonstrate serum to plasma equivalency. This shall be demonstrated for at least 50 sets of specimen.

IX. Devices intended for use with plasma, the performance evaluation shall verify the performance of the device using all anticoagulants which the manufacturer indicates for use with the device. This shall be demonstrated for at least 50 sets of specimen.

X. Devices should be subject to risk analysis and the whole system failure rate leading to false-negative results shall be determined in repeat assays on low-positive specimens.

XI. For import of HIV in vitro diagnostic reagents, comparison tests must be

conducted with similar products that have been approved for marketing domestically or in at least one countries out of the United States, Japan, Canada, Switzerland, Australia and the European Union. Six samples or more of HIV-1 Group O is recommended or relevant device design process of HIV-1 Group O antigens shall be submitted. With limited domestic cases of AIDS, IVD for HIV diagnosis developed domestically, MOHW shall review the submission on a case by case basis depending on the development process and method for measuring the sensitivity. The manufacturers can be requested to perform comparison testing overseas, and for IVD that screen against blood donors, test report against at least 6 samples of HIV-1 Group O or to include Group O antigen in the IVD design.

XII. For device intended for assay against HBsAg, independent of the testing principle and method, the analytical sensitivity shall be expressed in terms of the Second International Standard for HBsAG, subtype adw2, genotype A, NIBSC code: 00/588 or WHO International standards that can be traced back to the aforementioned standard must be "less than or equal to 0.130 IU/mL."

XIII. For HBeAg device, it shall not be tested by reverse passive hemagglutination method (RPHA).

XIV. For device intended for assay against HIV-1 antigen, the analytical sensitivity shall be expressed in terms of the concentration of HIV-1 p24 Antigen, 1st International Reference Reagent, NIBSC code: 90/636 or WHO International standards that can be traced back to the aforementioned standard must be "less than or equal to 2 IU/mL."

XV. For device intended for assay against Anti-HBs analytical sensitivity shall be expressed in terms of the concentration of WHO 1st International Reference Preparation 1977; NIBSC, United Kingdom or WHO International standards that can be traced back to the aforementioned standard must be

“less than 10 mIU/mL."

Article 8 Additional requirements for nucleic acid amplification techniques (NAT):

I. For target sequence amplification assays, there should be an internal control for each specimen tested to reflect the status of analysis.

II. Genotype detection shall be demonstrated by appropriate primer or probe design validation and shall also be validated by testing characterized genotyped samples. These information shall be submitted as necessary.

III. Quantitative NAT assays shall have results traceable to international standards or calibrated reference materials, if available, and be expressed in international units (IU) utilized in the specific field of application.

IV. Because the mechanism of the immune complex and free virus may be different, the robustness study must include pre-sero-conversion samples.

V. For investigation of potential carry-over, at least five runs with alternating high-positive and negative specimens shall be performed during robustness studies. The high positive samples shall comprise of samples with naturally occurring high virus titers.

VI. The whole system failure rate leading to false-negative results shall be determined by testing low-positive specimens. Low positive specimens shall contain a virus concentration equivalent to three times the detection limit of the virus concentration.

VII. The ability to detect mutants and different geno-diversity shall be demonstrated, where necessary.

VIII. If the tests system does not include sample pretreatment reagents (e.g., nucleic acid purification or bisulfite conversion reagents, etc.), evaluate the effect of chosen pretreatment methods with respect to satisfactory nucleic acid quantity and quality for the intended use should be provided. Using the recommended pretreatment reagents (including procedures) to evaluate the

test system's analytical and clinical performance.

Article 9 The manufacturing and purification process of final product.

For class III IVD, a complete and detailed description of the control of the manufacturing process shall be submitted accompanying the relevant SOP.

I. Flow Charts: A complete representation and description of the manufacturing process flow shall be submitted.

II. Raw Materials and Substances

(I) A list of all components used in the manufacturing process, their qualifying tests and specifications, or reference to official compendia, shall be submitted. For purchased raw materials, representative certificates of analysis from the supplier(s) and in-house acceptance testing results shall be submitted.

(II) A list of qualifying tests, test results and acceptance criteria for all special reagents and materials used in the manufacturing process, e.g., culture media, diluents, dyes, reagents, buffers, sera, antibiotics, monoclonal antibodies, preservatives shall be submitted. In some cases (e.g., if peptide or monoclonal antibody is used as raw material or semi-finished product), a detailed description of preparation and characterization shall be provided.

(III) Control of raw materials, reagents and components of animal origin: Information or certification supporting the freedom of substances from harmful agents, e.g., Bovine Spongiform Encephalophathy agent (BSE) or virus of animal origin, shall be included in the submission, if raw material of animal origin is used in the production process.

III. Manufacturing process: Safety related information as according to the origin of the raw materials shall be provided:

(I) Animal Sources: Information submitted concerning animals used in manufacturing, such as mice used for ascites production, rabbits used for

serum-antibody production, or transgenic animals, shall include detailed information on the following:

1. source and type of animals used (if transgenic, include the method of creation and the genetic stability)
2. harmful agents screening and the quarantine procedures used
3. specify geographic source and location of herd(s) for bovine products
4. immunogens used

(1) immunogenicity
(2) Specificity
(3) Purity
(4) sterility
(5) Stability
(6) immunization type, dose and schedule
(7) adjuvant if any

5. Description of substance of interest harvested from the raw material

(1) collection method, volume, receptacle, and schedule
(2) description of processing steps and components
(3) testing performed (titer/potency, affinity, specificity, sensitivity, bioburden, stability)
(4) storage conditions
(5) other characteristics unique to the raw material, process or intended use.

(II) Human Sources The information submitted concerning the use of source material of human origin shall include, but is not limited to, the following:

1. donor suitability/acceptance criteria
2. collection method, volume, and receptacle
3. anticoagulants used
4. description of component of interest
5. component processing

6. testing performed

(1) infectious disease marker tests

(2) titer (potency)

(3) affinity

(4) Specificity

(5) sensitivity

(6) bioburden

(7) Stability

7. purification and inactivation procedures
8. storage conditions
9. viral inactivation procedures
10. immunization dose and schedule
11. other characteristics unique to the raw material, process or intended use.

(III) Cellular Sources The information submitted concerning the use of source material of cellular origin, e.g., in monoclonal antibody or recombinant DNA technology, shall include, as appropriate, but is not limited to, the following:

1. source and type of cells
2. phenotype and genotype of cells
3. characterization of the parent cell line
4. cloning procedures
5. immortilization procedures
6. testing and monitoring procedures
7. characterization of gene construct
8. characterization of vector
9. establishment, characterization, maintenance, and stability of cell banks
10. cell culture procedures
11. harvesting procedures

12. purification and inactivation procedures
13. downstream processing procedures
14. other characteristics unique to the raw material, process or intended use.

(IV) Synthetic Sources Information shall be submitted concerning the use of materials from synthetic sources, e.g., synthetic peptides. The information submitted shall include, but is not limited to, the following:

1. Name:
2. Molecular formula
3. Chemical structure
4. Sequence
5. Purification procedures
6. Purity
7. Stability
8. Specificity
9. other characteristics unique to the raw material, process or intended use.

Article 10 Process Control or Batch Production Records

Process control procedures and complete batch production record/device history record of the entire process of manufacturing and testing shall be submitted.

I. In-process Controls

A description of the methods used for in-process controls, i.e., monitoring, testing, etc., used to assure that the functional requirement of the final product is met, e.g., integrity of solid-phase coatings, purity of enzyme labeled antibody/antigen conjugates, and potency, shall be submitted.

II. Process Validation

A description and the results of the process validation studies shall be submitted. If the manufacturing process was changed or scaled-up for

commercial production and involved changes in the manufacturing steps, the re-evaluation of the process shall be described, and the data and results provided. The description shall include studies for the following processes which identify critical parameters to be used as in-process controls to ensure the success of routine production.

III. Validation studies shall be submitted for the following:

(I) cell growth and harvesting processes

(II) purification processes

(III) inactivating or removing any infectious pathogens from materials used in the manufacturing process

(IV) to demonstrate microbiologic control over those processes susceptible to microbiological contamination for substances labeled as sterile or where preservatives are used.

(V) solid-phase coating processes

(VI) conjugation or derivation processes

(VII) potency adjustments

(VIII) Other

Article 11 Stability

I. Stability test report for 3 batches of finished products and semi-finished product shall be submitted. Real time stability test information shall be provided, and can be supplemented with relevant reference report and testing report of accelerated stability study for review. MOHW has issued a public announcement on Stability Testing for Pharmaceutical, and is recommended for planning of the stability study implementation.

II. A description of stability study protocol and results shall be provided for supporting the proposed storage conditions and shelf-life. This shall include information on the stability of intermediate fluids, labeled dilutions or formulated bulk under specified holding or shipping

conditions, as appropriate.

III. The devices shall be designed, manufactured and packed in such a way that the characteristics and performances during their intended use will not be adversely affected under storage and transport conditions (temperature, humidity, etc.) taking account of the instructions and information provided by the manufacturer.

IV. Storage instruction for maintaining the stability shall include temperature, light and humidity or other conditions.

V. A description of the container and closure systems, and their compatibility and biological tests with the final product should be provided. Evidence of container and closure integrity shall be provided for the duration of the proposed expiry period.

Article 12 Analytical Method Validation Information on methods validation and data analysis shall be submitted. This can be the pre-clinical performance testing

Article 13 Clinical Evaluation

I. Information on the product clinical evaluation, e.g. reproducibility, sensitivity, specificity, cross reactivity shall be submitted for review.

II. Clinical performance evaluation may be carried out in direct comparison with a device, which is currently marketed in Taiwan or one of the following countries or areas: United States, Japan, Canada, Switzerland, Australia, or European Union.

III. If discrepant test results are identified as part of an evaluation, these results shall be resolved as far as possible, for example:

(I) by evaluation of the discrepant sample in further test systems,

(II) by use of an alternative method or marker,

(III) by a review of the clinical status and diagnosis of the patient, and

(IV) by the testing of follow-up-samples.

IV. Positive specimens used in the performance evaluation shall be selected to reflect different stages of the respective disease(s), different antibody patterns, different genotypes, different subtypes, etc.

V. Devices shall be evaluated to establish the effect of potential interfering substances, as part of the performance evaluation Potential interfering substances shall be identified as part of the risk analysis required by the essential requirements for each new device but may include, for example:

(I) specimens representing “related” infections,

(II) specimens from multipara, i.e. women who have had more than one pregnancy, or rheumatoid factor positive patients,

(III) for recombinant antigens, human antibodies to components of the expression system, for example anti-E.coli, or anti-yeast,

VI. Clinical evaluation performed domestically:

Clinical evaluation of IVD does not fall within the scope of clinical trial as defined in Article 8 of Medical Care Act, and is eligible for simplified review process of IRB. The conducting of clinical evaluation for IVD domestically shall comply with Good Clinical Practice for Medical Devices, Guidelines on Collection and Use of Specimen from Human for Research Purpose, relevant regulation on medical device clinical trial announced by MOHW, and the following requirements:

(I) Beside the submission of performance evaluation information, tests for HBV, HCV and new IVD that is used in screening of blood donors, the clinical evaluation conduct domestically shall adhere to the following requirements:

1. It should be compared with similar products that have been approved for marketing in Taiwan. If there are no similar products approved for marketing in Taiwan, it must be compared with similar products approved for marketing in at least one of the countries out of the United States, Japan, Canada, Switzerland, Australia and the European Union.

2. In the comparison, if there is any deviation, another verification test shall be used such as Western Blot or clinical diagnostic tests.
3. The design and results of clinical evaluations shall be able to show or prove the substantial equivalency of the products.
4. Clinical evaluation shall be conducted from any 3 of the following institutions, Taipei Blood Center of the Blood Services Foundation, Kaohsiung Blood Center of the Blood Services Foundation and teaching hospitals, and at least 200 samples are tested at each of the selected institutes, including both positive and negative specimens. In cases where positive or negative specimens are difficult to obtain, an International panel should be used instead,
5. With the exception of new IVD that related to public health or blood safety, whereby MOHW could request the submission of protocol for review, otherwise clinical evaluation can be conducted after the approval of IRB of the evaluation institutions and do not have to first submit the proposal to MOHW for review.
6. Collection of Specimen for the clinical evaluation shall be done according to the "Guidelines on Collection and Usage of Human Specimen" announced by the MOHW.
7. When conducting clinical evaluation, consideration shall be given to the operational biosafety at the location, and shall carry out the appropriate safety measures.
8. For comparison of IVD for hepatitis against a similar product, the specificity should not be differ by more than 2%.

(II) For IVD other than above mentioned, the number of samples used for clinical evaluations shall be depending on the characteristics of the product and calculate using statistical tools and method. The

calculation of sample number and relevant references should be provided by the manufacturer. MOHW recommends that the number of clinical evaluation samples should have at least 80% of the statistical power to support the declaration of performance, or to use other method to establish the number of samples for clinical evaluation. The number and profile of specimens in the clinical evaluation report shall be adequate to support the declaration of test item and performance stated on the instruction. After reviewing the clinical evaluation report, MOHW can request for clinical evaluation conducted domestically for IVD performance that can have racial or geographical variance.

(III) MOHW encourages clinical institutions and clinical evaluation laboratories, management, quality control and research professionals to follow Good Laboratory Practice (GLP) of MOHW and to apply for voluntary GLP audit.

Appendix I. Labeling and packaging information

1. Name and address of the manufacturer. For devices imported into Taiwan, it should clearly labeled with the name and address of the importer and the original manufacturer;
2. Details necessary for the user to uniquely identify the device and the contents of the packaging;
3. Labeling with the word ‘STERILE’, where appropriate;
4. Lot No.
5. Date of manufacture and expiration period or the storage period and storage condition should be labeled on the product. If appropriate, an indication of the date by which the device or part of it shall be used, in safety, without degradation of performance, expressed as the year, the month and, where relevant, the day, in that order;
6. The statement “For In Vitro Diagnostic Use” indicating the in vitro use of the device;
7. Storage and/or handling conditions;
8. Operating instructions;
9. Warnings and/or precautions to take;
10. Indication for self-testing, if appropriate.

References

1. Guidance for Industry and FDA Staff: Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use, FDA/CDRH/CBER, November 30, 2004
2. Guidance on Medical Device Patient Labeling; Final Guidance for Industry and FDA Reviewers, FDA/CDRH, April 19, 2001
3. Guidance for Industry: Content and Format of Chemistry, Manufacturing and Controls Information and Establishment Description Information for a Biological In Vitro Diagnostic Product, FDA/CBER, Mar. 1999
4. Guideline for the Manufacture of In Vitro Diagnostic Products, FDA/CDRH, January 10, 1994
5. Requirements for Immunoassay Kits, WHO Technical Report Series, No.658, 1981. p.206-242
6. Commission decision of 7 May 2002 on common technical specifications for *in vitro*-diagnostic medical devices, European communities 2002/364/EC
7. GHTF/SG1/N41R9;2005 Essential Principles of Safety and Performance of Medical Devices, The Global Harmonization Task Force May 20, 2005
8. GHTF/SG1/N46:2008 Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices, The Global Harmonization Task Force July 31, 2008
9. Directive 98/79/EC of The European Parliament and of The Council of 27 October 1998 on *in vitro* diagnostic medical

devices

10. Commission decision of 27 November 2009 amending Decision 2002/364/EC on common technical specifications for *in vitro*-diagnostic medical devices, European communities 2009/886/EC

11. Corrigendum to Commission Decision 2009/886/EC of 27 November 2009 amending Decision 2002/364/EC on common technical specifications for in vitro diagnostic medical devices

12. GHTF/SG1(PD)/N063 Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices, The Global Harmonization Task Force March 26, 2009

13. GHTF/SG1/N43:2005 Labelling for Medical Devices, The Global Harmonization Task Force June 3, 2005