Regulations for Registration of Medicinal Products

Chapter 1 General Principles

Article 1

The Regulations are established pursuant to Article 39 Item 4 of the Pharmaceutical Affairs Act (hereafter the Act).

Article 2

The registration of drugs, and the post-approval change, transfer, extension, or reissue of damaged or lost drug licenses should follow the Regulations. Matters not included in the Regulations are subject to other regulations, orders or announcements made by the central health competent authority.

Article 3

For the registration items mentioned in the preceding article, the applicant should pay the application fees and submit completed application forms and all required dossiers to the central health competent authority for assessment.

The above-mentioned application forms and documents include those for drug review and registration, post-approval changes, extension of validity of drug license, assurance statement, sticking label and package insert, sticking licenses and certificates, and other forms and documents in relation to the application procedure.

“Chinese language” in the Regulations denotes traditional Chinese. For forms and documents requiring Chinese language, please provide information in traditional Chinese characters or documents with translations in traditional Chinese characters.

The license holder may retain the original certificates for future inspection when submitting an application via an electronic system, but needs to submit the original drug licence to the central health competent authority to have the approval status marked on the licence.

Chapter 2 Western Medicine

Section 1 General Provisions

Article 4

The terms used in this chapter are defined as follows:

1.New drugs: the new drugs described in Article 7 of the Pharmaceutical Affairs Act.

2.Generic drugs: pharmaceutical preparations identical to a drug already approved in Taiwan in the aspects of ingredients, dosage form, contents and efficacy.

3.Bio-pharmaceuticals: serum, antitoxin, vaccines, toxic, bacteria sap and products manufactured based on the theories of microbiology and immunology.

4.Substances (Active pharmaceutical ingredients): An active substance or ingredient manufactured through physical and chemical processes or bio-tech procedures and with pharmacological effects that are often used for the manufacturing of drugs,

bio-pharmaceuticals or bio-tech products.
5.Radiopharmaceutical drugs: drugs meeting the definition given in Article 6, containing radioactive substances for human uses. After being administrated to humans, the drug can diagnose, monitor, treat, alleviate disease conditions or achieve other medical effects.

Article 5

The term “authorization letter” mentioned in this Chapter refers to the documents issued by the foreign manufacturer, headquarters or the license holder of an imported drug to authorize the application of drug registration.

The above-mentioned authorization letter is effective for one year from the issuance date. The authorization letter should include the names and addresses of the manufacturer and the agent, as well as drug name, dosage form and contents. The information should be consistent with those stated in the application form. If the authorization letter is in neither Chinese nor English, a Chinese or English translation should be provided additionally.

If the original license holder has a branch office in Taiwan, the authorization letter can be issued by either the manufacturer’s headquarters or the head office in Asia.

Article 6

The FSC (Free Sales Certificate) from the country of origin mentioned in this Chapter means the original document issued by the highest health competent authority of the country of origin, therein justifies the manufacture and sale of the product in that country. The following conditions should be met:

1.If the required document is in neither Chinese nor English, a Chinese or English translation should be provided additionally.

2.The document is effective for two years from the issuance date, and it should be authenticated by the embassy, representative office or agencies authorized by the Ministry of Foreign Affairs of R.O.C (hereafter the R.O.C foreign affairs offices).The authentication requirement is waived for documents issued by A10 countries, which include Germany, US, UK, France, Japan, Switzerland, Canada, Australia, Belgium, and Sweden.

3.Information of the product name, manufacturer’s name and address, drug formulation, dosage form and contents stated on the document should be consistent with the information on the application form. The product name of exporting drug should be stated in this document; otherwise, a letter issued by the original manufacturer should be provided to explain and to give the product name of exporting drug, as well as to certify that the product is consistent with every description on the CPP (Certificate of Pharmaceutical Product) except for the product name. For capsules, in addition to the full formulation of the drug, the full

formulation of soft capsule, or the coloring agents of hard capsule should be described accordingly. In cases where the CPP does not state the coloring agents of hard capsule, the original manufacturer should issue a letter to explain.
4.The CPP should specify the drug manufacturer and state the fact that the product has been approved for free sale in that country. The description of manufacturing and free sale should be clear.
The following documents can substitute for the above-mentioned FSC from the country of origin:
1.FSC issued by the selling countries approved by the central health competent authority;
2.For drugs listed in the United States Pharmacopeia Drug Information (USPDI) or in the Approved Prescription Drug Product with Therapeutic Equivalence Evaluations (Orange Book) published by the US FDA, applicants may submit a photocopy of the pages of the product (printouts from the Internet or the electronic version are acceptable), as well as the FSC issued by the health authority of the State Government as a replacement for the one issued by the US FDA;
3.For products manufactured in Germany, the FSC can be issued by the health authority of a state government. Notarization from the Federal Government would not be necessary;
4.For products manufactured in any of the EU countries, the FSC issued by the European medicinal Agency (EMA) is acceptable; and
5.For toll-manufactured products that have not been sold in the country where the toll-manufacturers are located, the FSC from the country where the commissioner is located together with the manufacturing license from the country where the manufacturing takes place are acceptable substitute. Another acceptable alternative is the FSC from the country where the commissioner is located, on which states the manufacturer’s name and address.
Except as otherwise regulated in the Regulations, Paragraph 1 Item 1 to Item 4 are applicable to the above-mentioned alternative documents and the certificate of changes issued by the country of origin.
Article 7
Except as otherwise regulated in the Regulations, the CPP said in this Chapter should be issued by the highest health competent authority of the issuance country and authenticated by the R.O.C. foreign affairs offices. The authentication requirement is waived for documents issued by A10 countries.
The CPP said in the preceding paragraph refers to the CPP issued by any one of the A10 countries, or the CPP issued by the EMA (European Medicine’s Agency).
CPP can be replaced with the package insert approved by the reference country or a

photocopy of the reference country's pharmacopoeia (as listed below, as "official formulary"); printouts from the Internet or the electronic version are also acceptable. It does not have to be issued by the highest health competent authority of the reference country, nor be authenticated by the R.O.C. foreign affairs offices. The edition of the cited official formulary should be indicated, and has to be published within 5 years from the citation.

1.US: Physicians' Desk Reference (PDR);
2.UK: British National Formulary (B.N.F.), Medicines Compendium (published by Association of British Pharmaceutical Industries, ABPI);
3.Japan: Drugs in Japan, the most recent new drugs in Japan;
4.Switzerland: Arzneimittel-Kompendium der Schweiz;
5.Canada: Compendium of Pharmaceuticals and Specialties;
6.France: Dictionnaire VIDAL;
7.Australia: MIM'S;
8.Germany: Rote Liste;
9.Belgium: Repertoire Commente des Medicaments;
10.Sweden: Farmaceutiska Specialiteter i Sverige (FASS).

Article 8

Except as otherwise regulated, the formulation basis mentioned in this Chapter refers to the pharmacopoeia or official reference books published in the A10 countries of editions published within 5 years from the date of application. Formulation basis should meet the following criteria; its title, edition, year of publication and page numbers should all be indicated. A photocopy of complete reference pages should be provided. If the reference is in neither Chinese nor English, a word for word Chinese translation should be provided; but proper names or technical terms can be listed in English.

1.If USP is submitted, then the USPDI shall also be provided for assessment. Extra pharmacopoeia, which is not an official reference book, is for reference only.
2.If the applied formula is not completely consistent with the submitted reference and some alternations have been made, a statement explaining the alternation should be provided. Information in relation to the actual changes should be submitted as appropriate.
3.Tablets, film-coated tablets and sugar-coated tablets can use the same formulation basis, but not for enteric-coated tablets.
4.The formulation basis of ointment and cream can be used interchangeably, provided that the products are not under pharmacovigilance.
5.If the formulation basis or the CPP is of tablets, the reasons for the application of double-layered tablets should be given. Moreover, the package inserts and labels

shall not include exaggerated therapeutic effects associated with the dosage form. Any boost of effects due to dosage forms should be approved and justified by clinical data before they can be indicated in package inserts or labels.

6.If the formulation basis submitted by local manufacturers for drug registration is not pharmacopoeia or reference books published by the A10 countries, the Orange Book or USPDI published by the US FDA can be used instead.

New drugs, new dosage forms, new administration doses or new unit strength developed in Taiwan do not need to submit formulation basis. However, the researches of formulation design and technical data in relation to this drug should be submitted.

Article 9

The testing specifications, methods and certificate of analysis of raw materials mentioned in this Chapter refer to those for active pharmaceutical ingredients (API) and every substance of the formula (including auxiliary materials and coloring agents added during the manufacturing process).

The testing specifications, methods and certificate of analysis of raw materials should comply with the following regulations:

1. If using a pharmacopoeia as a reference for raw materials, the applicant should indicate the pharmacopoeia's titles, publication year, editions and page numbers. The pharmacopoeia is restricted to the Chinese Pharmacopoeia, pharmacopoeias published by the A10 countries, or pharmacopoeias approved by the central health competent authority. The cited edition should be published within the last 5 years.
2. New chemical entities (NCE) are subject to the regulations set by the manufacturers.
3. The reference standards for tests should be indicated whether they are Primary Standard or Working Standard. For Primary Standard, the source should be specified. For Working Standard, the source, batch number, labelled content (or potency), testing specifications, certificate of analysis and calibration procedures should be specified.
4. For coloring agents, testing specifications and methods should be indicated. Testing specifications are not required for aromatics.
5. The certificate of analysis justifying every formulation substance should be the certificates about the substances of the same lot as the finished products.
6. Raw materials should be tested against each specification item. Documented operational procedures of items exempted from tests should be submitted, along with the certificates of analysis of the batch subject to full tests.
7. If test results are in numerical figures, then keep the original data in the document; if the test is a comparison with reference standard, then use "pass" to indicate a

satisfactory result.

Article 10

The testing specifications, methods and certificate of analysis of finished products mentioned in this Chapter refer to those performed on pharmaceutical preparations. The regulations of testing specifications, methods and certificate of analysis of finished products are as follows:

1.If the applied drugs are listed in pharmacopoeias, the testing specifications attached to the application form should include the pharmacopoeia's titles, publication year, editions and page numbers. Such reference is restricted to the Chinese Pharmacopoeia, pharmacopoeia published in the A10 countries or acknowledged by the central health competent authority in Taiwan. The publication year has to be within 5 years from the date of application. If the item in the pharmacopoeia includes more than two esters or salts, or contains ingredients with crystallized water or anhydride, the applicants should clearly specify which one is applicable to this application. In vitro pyrogen test methods should be considered alternatives for animal tests.

2.For each active ingredient, the applicant should state its standard test scopes and methods in the testing specifications. Denotation of the identification and assay of the contents should not be simply summarized as "operated according to certain pharmacopoeias".

3.If necessary, upon the request of the central health competent authority, the applicant should provide test records, including the information listed below and all test data to justify whether current regulations and criteria have been met:

(1)Sampling venues, quantity, batch numbers or other specific codes, the date of sampling and the date when tests were completed;

(2)References to justify every test method;

(3)The weight or volume of samples for each test;

(4)The reference standards for each test should be indicated whether they are Primary Standard or Working Standard. For Primary Standard, the source should be specified. For Working Standard, the source, batch number, content (potency), test specifications, certificate of analysis and calibration procedures should be specified;

(5)Complete data records produced from each test, including equipment output charts and spectrums, etc. All data should be clearly described to avoid confusion;

(6)All calculation records associated with tests;

(7)Conclusions on the comparison between test results and existing specifications;

(8)For every test, the names of the persons performing the test and the date of the test;

(9)Signatures from reviewers who have checked the original records for accuracy,

safety and the compliance with existing specifications.
4.Provisions set out in Paragraph 2 Item 5 to Item 7 of the preceding article are applicable to the certificate of analysis of finished products.
For toll-manufactured pharmaceutical products, the tests of finished products should comply with the Guidelines on Toll-Manufacturing and Contract Testing of Pharmaceutical Products. The purpose of those tests is to ensure drug quality. Tests can be performed by the commissioned toll-manufacturers.
Article 11
The manufacturing records mentioned in this Chapter refer to the manufacturing records of the same lot as the samples submitted for tests. In the case where the data of the same lot is not available or the products are exempt from testing, the applicant can submit the manufacturing records of any batch produced within two years from the date of application.
The Manufacturing and Control Standard mentioned in this Chapter refers to the Manufacturing and Control Standard in compliance with Part 2 of Good Manufacturing Practice Regulations (Good Manufacturing Practices for Pharmaceuticals), including data of the actual amount of material used in batch records.
Article 12
The term “changed licenses” mentioned in this Chapter includes supporting documents of factory registration, drug company licenses and certificates or official documents of company registration and business registration.
Photocopies or photos of the following documents shall be affixed on the form:
1.Drug company license;
2.Supporting documents of factory registration (imported drugs are exempted); and
3.Certificates or official documents of company registration or business registration.
Article 13
The original references of data submitted to support the application should be provided, including physicochemical characteristics, pharmacological and toxicological test data, pharmacokinetic data, bioavailability rate, documents of clinical usage and other research reports. They can not be substituted by general descriptive information, summarized data or case reports. If the original references are in neither Chinese nor English, then a translation version in Chinese or English should be submitted along with the translators’ names.
Article 14
Product names should comply with the following regulations:
1.Do not use the other manufacturer’s name or trademark as a product name, except in the case the use has been authorized;

2.Products named after items in pharmacopoeias, common names or conventional formulas should include the company's name or trademark or any distinguishable title as a prefix; but, this naming rule does not apply to export only products;
3.Product names can not be identical to any other exiting product names. Counterfeiting or insinuation is not allowed;
4.Product names should not be deceitful or exaggerated, nor should they give any misinterpretation on product efficacy;
5.Chinese product names should not include any foreign letters or numbers, unless therein lies real meanings;
6.For drugs whose licenses have been revoked pursuant to the Acts, their product names are banned from use for two years; but, this two-year ban does not apply to the following situations: the application is a re-submission according to the condition stated in Article 72 Paragraph 1; or, the original license is changed to export-only license; or, the reasons of the revocation or cancellation of an export-only license are irrelevant to drug safety or effectiveness. With the central health competent authority's approval, the manufacturer can name the drugs with identical ingredients, dosage form, dose and efficacy for the original names.
7.If a manufacturer gave compounds with different formulas the same product name, then their Chinese product names should contain proper words or terms to clearly distinguish their differences in efficacy; and
8.Names that are inappropriate for pharmaceutical products shall not be used.
In order of priority, whether product names are identical or similar is judged on trademarks, the manufacturer's name and other distinguishable names. However, in the situation described in Item 3 in the preceding paragraph, the manufacturer's name and trademark will not be included in the comparison.
For drug items already granted with market licenses, the central health competent authority may reassess their product names pursuant to the previous two paragraphs.
Article 15
Drug packaging materials and the data field of packaging on the application form should comply with the following regulations:
1.The quantity, materials and types of the drug packaging should be specified;
2.Except for oral nutrient liquids, all bottled solutions for oral internal use and syrups, shall not be packed in ampoule. The volume should be indicated on each bottle; and
3.The unit recorded in the data field of packaging on the application form should be identical to the unit dosage form of the formula.
The maximum package size for drugs should follow the standards in the Table of Maximum Package Size. If there are any special purposes for the maximum package

size, the purposes should be stated on the packaging. For common pharmaceutical preparations, the minimum package size is the two-day dose for an adult. For syrup containing codeine (phosphate) as an instruction drug, the maximum package size is the three-day dose. Tablets or capsules containing ephedrine or pseudoephedrine should only be packed in aluminium blister foils and boxes. For instruction drugs, the maximum package size is the seven-day dose for an adult. For drugs for the cold, fever, pain relief and for the cough liquid, the package size should be between one single adult dose and 4000 ml. The restrictions do not apply to sickness drugs and pesticides.

Please see Appendix 1 for the Table of Maximum Package Size as mentioned above.

In the situation where the packaging is over its maximum package size, an application to change the registration should be made by providing documents of purchasing orders from health care providers or academic institutes. The application for changes does not apply to instruction drugs containing ephedrine or pseudoephedrine.

Appendix 1.PDF

Appendix 1.doc

Article 16

The applicant should honestly and completely fill out the application form, including the company name, code, address, telephone number, drug company license number, the person in charge of the business, the pharmacist in charge of the management or manufacturing, and the pharmacist's address, and license number. The information should be confirmed by using private signets.

The same signets or stamps used in the application form should be used for any follow-up applications. The applicant should report to the authority if the signet or stamp is lost.

In the situation of toll-manufacturing, the names, codes and addresses of all manufacturers involved in the manufacturing processes should be listed in the data field of manufacturers on the application form.

Article 17

The information given in the data fields for raw materials and contents on the application form should comply with the following regulations:

1.The contents of the formula should be indicated per minimum unit;

2.The contents should be in International System of Units (SI), without including the increasing rate;

3.For pharmaceutical preparations containing ingredients of crude drug, the active ingredients in the formula should be listed in the order of chemical ingredients and the ingredients of crude drugs;

4.Solvent, auxiliary solvent, stabilizers and other excipients used for injections should

be described in detail and be suitable for injection. The contents of the formula should be indicated per minimum unit. However, for powder or lyophilized injections, the contents can be indicated per minimum package size;
5.The English names and contents of aromatics, coloring agents, preservatives and other excipients should be indicated;
6.Artificial flavouring may be added if the use is medically justified, but it shall not be added to the nutrient liquid;
7.For capsules, in addition to the full formula of the drug, a description of the full formula of soft capsules, and coloring agents of hard capsules should be described accordingly;
8.The ingredient and contents of active pharmaceutical ingredients should be described in a way consistent with the method used in a pharmacopoeia;
9.If the item includes more than two esters or salts or contains ingredients with crystallized water or anhydride, the applicant should clearly specify which one is relevant to this application;
10.The sources of active ingredients of drug products (manufacturers' names, manufacturers' addresses and the country of origin) should be specified. Source data can be declared electronically after the approval of the registration.

Article 18

The information given in the data field of indications on the application form should be based on the drug efficacy or indications approved by the central health competent authority, including the drug re-categorization, drug re-evaluation results, and the Guidelines on the Review of Instruction Drugs.

When filling in the information of drug efficacy and indications, in addition to following the regulations stated in the preceding paragraph, the applicant can also provide a summary by taking references from information on new drugs and new indications and formularies of the A10 countries. If there are any changes in efficacy, related information should be provided for review.

Article 19

Assurance Statements (A) and (B) attached to the application form should include the company name, address, person in charge and the date of signature. The information should be confirmed by using the same signets or stamps as those for the application form. In the situation of toll-manufacturing, assurance statements from both the appointer and the appointee are required.

Article 20

Drug labels, package inserts and packaging are subject to Article 75 of the Regulations, and can contain only the information approved by the central health competent authority. The statutory contents and presentation should comply with

the following regulations and the print should be easy to read:
1.Package inserts should include information on drug category, packaging, storage and all compulsory matters required by other regulations;
2.The outer packaging of imported drugs should meet the following conditions:
(1)The Product name, active ingredients and contents, and the name and address of the manufacturer or company should be printed by the original manufacturer. If the manufacturer's name and address is not printed on the outer packaging, this information should be printed on a sticker adhering to the outer packaging;
(2)The company name, address and license number of the drug company, drug category and Chinese product name can be provided on a sticker;
(3)If the information of the manufacturer's name and address is not printed on the outer packaging by the original manufacturer, it may be printed on a sticker with the information as stated above in the preceding item (2); and
(4)For toll-manufactured products, with approval from the central health competent authority, the appointee's name and address can be substituted by the country from where the appointee is located.
3.For generic drugs under pharmacovigilance, the package inserts should follow that of the first approved drug. For generic drugs not under pharmacovigilance, the package inserts should be a precise translation of the package inserts of the original drugs.
4.The process of labelling is deemed a part of the manufacturing process and is subject to GMP Guidelines. For imported drugs, labelling should be done by the original manufacturer. Packaging and labelling can be commissioned to a GMP manufacturer or a GMP medical product distribution center in Taiwan, pursuant to the Guidelines on Drug Toll-Manufacturing and Contract Testing. Information about the GMP manufacturer or GMP medical product distribution center in Taiwan which packages and labels drugs in accordance with this paragraph may be exempted from the stickers.
5.Outer packaging and the immediate packaging have to be labelled in Chinese and English, pursuant to this article. If the immediate packaging does not have enough space to include information in both languages, at least product name and contents in Chinese should be provided. Labels listed below are deemed in compliance with this Paragraph.
(1)Injections that are packed in one injection per box for single use with Chinese information printed on outer packaging;
(2)Drugs that are sold or dispensed in original packaging with the outer boxes remaining intact, on which Chinese information is printed; or
(3)Drugs that are classified by the central health competent authority to be used only

by physicians with outer boxes printed with Chinese information.
6.For the following drug items, if Chinese information is provided on outer boxes, then only the Chinese or English product name and contents are required on the immediate packaging to meet the regulations in the preceding paragraph.
(1)Drugs for rare diseases;
(2)In situations where special storage conditions are required, i.e. drugs that need to be refrigerated or frozen; or
(3)Special cases that the central health competent authority's approval on drugs is required.
7.In principle, the information on package inserts should be within the pharmacological scope of its active ingredients and major efficacy. For compound preparations, the scope should be within the scope of the major pharmacological functions of mixed active ingredients. Exaggerated terms and wordings are not allowed.
8.Contraindications, warnings, side effects, and precautions stated on package inserts should be indicated in detail and printed in red, framed in red line, or in boldface to attract the special attention of users.
9.Chinese characters should not be smaller than font size seven.
10.Drugs sold on the market may only provide approved Chinese package inserts. However, if both Chinese and English package inserts are provided, the contents of the English version should be consistent with that of the Chinese one. Manufacturers may of their own accord modify the contents of the English version to fit the Chinese version.
11.Package inserts, labels and packaging materials should not include photos or wordings that are indecent, offensive or exaggerated.
12.If the distributor's name is printed on the package inserts, labels or packing materials, the font size of the distributor's name should not be bigger than that of the manufacturer (license holder). A photocopy of the distributor's business license should be submitted for reference.
13.The font size of the Chinese product name should not be smaller than that in foreign language. The printing should be clear. As a standard for comparison, the height of the printing of product name in Chinese should not be lower than that in foreign language.
14.For OTC (Over-the-counter) drugs, the labels and packaging should include significant prints of the product category, i.e. OTC drugs or Class B OTC drugs. In principle, printing should be in regular fonts.
15.Whereas the active ingredients, dosage form, dose and administration route of a licensed drug remain unchanged, the appearances or shapes of its aromatics,

coloring agents or corrective agents without any pharmacological effects are altered but do not affect drug quality or medication safety, then it can be justified by applying for post-approval changes for excipients as the addition of new contents. Appropriate descriptions should be given on labels, package inserts and outer packaging for clear differentiation. Graphic designs and colors may be changed to suit the new descriptions.

16.For drugs packed in aluminium blister foils, each sheet of foil should be printed with the drug name using Chinese as the main language. Manufacturer's name and license number can be provided. The following conditions are deemed to meet the criteria of this Paragraph:

(1)The product name in Chinese has been printed on (or adhered to) the immediate packaging of each aluminium blister foil sheet;

(2)Drugs are dispensed or sold in original packaging with the outer boxes remaining intact, on which information in Chinese is printed.

17.Drug labels and packaging should contain information of batch number, manufacturing date, effective period and expiry date in any of the following format:

(1)batch number, manufacturing date and effective period;

(2)batch number and expiry date; or

(3)batch number, manufacturing date and expiry date.

18.The manufacturing date and expiry date as mentioned in the preceding paragraph should be written with Arabic numbers using four-digit format for year.When only month and year are shown for the expiry date,either year-month or month-year format is accepted. For manufacturing date and expiry date containing all three components (year,month,day), the date should be written in the year-month-day format (from left to right). If other date notations are used due to unavoidable circumstance,the format used (e.g., dd/mm/yyyy,day/month/year,etc.) should be clearly expressed on the outer box. But, for products whose validity period is over 2 years, the manufacturing date and expiry date can include year and month only and set at the last day of that labelled month as the expiry date.

19.Information of the materials that have direct contact with pharmaceutical products should be labelled on plastic containers of L.V.P. (large volume package) for infusion.

Statutory package inserts, labels, outer boxes, aluminium blister foils and other materials or graphic for labelling purpose should comply with the additional items required to be printed as announced by the central health competent authority, as well as the drug re-evaluation results, Guidelines on the Review of OTC Drugs, drug re-categorization and regulations of standardized package inserts.

In addition to the regulations set out in previous two paragraphs, the additional

printings on labels and packaging of controlled drugs should also comply with the Regulations Governing Controlled Drugs as well as other related regulations.
Actual printing materials or drafts of outer boxes, package inserts, labels, aluminium blister foils and other labelling materials should be adhere to the form for sticking label and package insert. If such forms are required for the application of drug registration or post-approval changes, then the actual materials or drafts of the packaging materials should be submitted. But, color pictures of aluminium blister foil can be used to substitute the actual materials.
When collecting license, applicant should submit the electronic files of the image of drug appearance, labels, package insert and packaging as approved by the central health competent authority. For applications of post-approval changes in drug appearance, labelling, package insert or packaging, electronic files of the new contents approved by the central health competent authority should be submitted.
Article 21
Validation requirements for medicinal product are described as follows:
1.When applying for drug review and registration, the applicant may firstly prepare the analytical method validation report and the protocol of the validation of critical manufacturing processes. After receiving approval, the manufacturer should conduct validation studies on three consecutive batches of products. If the results meet all specified criteria, the product can therefore be marketed.
2.The validation studies should be able to assure drug effectiveness and safety and comply with the Guidelines on GMP Validation Requirements as announced by the central heath competent authority.
3.The contents and schedule of a drug validation process are as follows:
(1)Manufacturers should submit the validation documents of the supporting system, equipment and facility, critical manufacturing processes (including cleaning validation) and analytical method of at least one product to the central health competent authority for inspection. The submission deadlines were 31 December 2000 for local manufacturers and 10 June 2002 for license holders of imported drugs. For those failing the submission or the assessment, the authority will make a public list of their company names and all their approved drug licenses in Taiwan, and give a deadline for improvement. These companies are not allowed to file any applications of new drug registration. Companies missing the deadline for improvement will be denied the rights to apply for license extension.
(2)Manufacturers should submit the validation documents of the critical manufacturing processes (including cleaning validation) and analytical method of all products to the central health competent authority for inspection. The submission deadlines were 30 June 2002 for local manufacturers and 10 December 2003 for

license holders of imported drugs. Companies failing the submission or the assessment will be handled according to the proceedings stated in item (1).
(3)Manufacturers should fully implement all validation processes and submit the documents to the central health competent authority for inspection. The deadlines for submission are 30 June 2004 for local manufacturers and 10 December 2005 for license holders of imported drugs. Companies failing the submission or the assessment will be handled according to the proceedings stated in Item (1).
(4)Validation would not be necessary for license holders that do not manufacture or import drugs to sell. This exemption took effect from 1 July 2002 for local drugs and from 11 December 2003 for imported drugs. However, licenses of imported drugs may be extended without validation, if the license holder submits the drug license and an assurance statement certifying that the drug will be imported for sale only after all validation documents have been submitted and approved. The license will be stamped, noting that the drug can not be imported due to deficiency of required documents. After all documents are submitted and approved, the license will be re-stamped, indicating that the drug can now be imported for sale on the grounds that full compliance has been met with the DOH's requirements.
(5)Penalties will be imposed on license holders pursuant to the Pharmaceutical Affairs Acts, if drugs have been produced or imported to sell without validation.
Article 22
The information and local clinical data required for the application of drug registration or post-approval changes should comply with the following regulations:
1.Clinical trials conducted in Taiwan should follow the regulations of the GCP (Good Clinical Practice) Guidelines, as well as the Notices for the Application of Clinical Trials and the Guidelines on Bridging Studies as announced by the central health competent authority.
2.Before conducting a clinical trial, the manufacturer should submit a protocol, a protocol summary and an application form to the central health competent authority for assessment.
3.After the application is approved by the central health competent authority and an official approval letter is issued, the manufacturer should carry out the clinical trial according to the comments provided with the assessment results. After the completion of the clinical trial, the results should be submitted for inspection.
Clinical data from foreign countries submitted together with the application should have a comparison with a control group or a double-blind test design. This data can not be substituted by a general descriptive document, summarized data or individual case report. The regulations set forth in the preceding item are applicable to the technical data of local clinical trials

Article 22-1

The following drug items are subject to a bridging study assessment:

1.New chemical entities (NCE); or

2. Genetically engineered drugs, vaccines, plasma derivatives of new molecular entities, and allergen extracts of new molecular entities; or

3.Items announced by the central health competent authority as requiring a bridging study assessment.

For drugs other than the two categories listed above, whether an application of a bridging study assessment shall be filed is left to the discretion of manufacturers. For applications without bridging study data, if the central health competent authority considers that a bridging study is necessary, the manufacturer is obliged to conduct a bridging study.

When applying for a bridging study assessment, manufacturers should fill out the checklist for bridging study assessments and provide a complete clinical data package, preferably with data on ethnic groups in Asia. Applications of bridging study assessments can be filed prior to or together with the applications of drug registration.

Bridging study data would not be required for the applications of drug registration that have been approved by the central health competent authority to be exempt from bridging studies. However, there should still be sufficient clinical data to justify drug efficacy and safety.

If the assessment result suggests that a bridging study is necessary, the applicant should prepare an appropriate protocol according to the comments from the assessment and submit the protocol to the central health competent authority for assessment. After the protocol is approved, the applicant should conduct the bridging study and submit study reports and related data to the central health competent authority for inspection.

In situation where a license is granted to a new drug with the submission of bridging study data, if in the next 5 years any generic manufacturer intends to manufacture or import generics with ingredients, dosage form and contents identical to this new drug, then the generic manufacturer should submit all required data and a bridging study report up to the standards set by the first license holder.

Article 23

If the application for drug registration concerns about a drug involved in toll-manufacturing or contract analysis, then the applicant should submit data required by the Guidelines on Drug Toll-Manufacturing and Contract Analysis and all related information required by Article 64 and Article 66.

Article 24

Except as otherwise regulated, all applications covered in this Chapter are subject to a parallel assessment of dossier review and drug testing. If the submitted dossiers pass the assessment, then the applicant should follow the notice issued by the central health competent authority to collect the license. Once the test specifications are approved, the applicant should follow the notice issued by the central health competent authority to proceed with drug testing.

The following applications only require dossier review, while drug testing can be exempt except for those cases deemed by the central health competent authority as drug testing being necessary.

1.Drug registration:

(1)Pharmaceutical preparations classified as OTC drugs (including Class B OTC drugs);

(2)Vitamins meeting the criteria for products containing vitamin substances;

(3)Generics;

(4)Pharmaceutical preparations meeting the criteria set out by the Guidelines on the Review of Over-the-counter Drugs;

(5)General active pharmaceutical ingredients; and

(6)Pharmaceutical preparations and active pharmaceutical ingredients for exportation only.

2.Post-approval changes

As mentioned in the preceding paragraph, for those drugs that only abide by dossier review, the applicant should submit color photos or scanned images of a sample product for assessment. If necessary, a reference standard should be provided for comparison.

Article 25

In any of the following situations, applications will be rejected:

1.Applicants don’t have the qualifications required, or manufacturing equipment does not meet the standard, e.g. hardware, software or dosage form equipment does not comply with GMP Guidelines; or there has been no submission of evidence to support compliance with related regulations;

2.No application fees have been paid, or the submitted data is insufficient or does not fit with the contents of the application;

3.The major efficacy of the applied drug is unclear or insignificant; or the drug fails the drug re-evaluation;

4.The applied drug has severe side effects or safety concerns;

5.The contents of toxins or controlled substances contained in the applied drug do not conform to regulated doses;

6.The applied drug contains unapproved coloring agents, preservatives or anti-oxidants;

7.The applied drug contains forbidden ingredients;
8.The applied drug has inappropriate formula, manufacturing method or dosage form;
9.The ingredients of an oral liquid product are not nutrients, or contain Caffeine-like substance;
10.Hormone (including anabolic hormones, steroid), stomachics, pesticides, sickness drugs or pharmaceutical preparations with effects of anti-sleep, antipyretic, antitussive, expectorants or other medical efficacy, that are registered in the dosage form of oral liquid;
11.Amino acid and multi-vitamin nutrition that in total contain over 8% w/v of alcohol;
12.Syrup containing codeine (phosphate) with the content of sucrose less than 55 w/v; or syrup categorized as Over-the-counter (OTC) drugs with the content of codeine less that 1g per 100ml and in compliance with the following rules about the content of codeine:
(1)The maximum daily dose is 9 mg for syrup for the cold and 18mg for syrup for antitussive or expectorants;
(2)For concomitant use with Ephedrine Hydrochloride, dl-Methylephedrine Hydrochloride, the dose should be reduced by 20%;
(3)The single dose for an adult should be at least 5ml; and the formula's unit strength should be adjusted accordingly.
13.Pharmaceutical preparations combined with Chinese traditional medicine and western pharmaceutical medicines that contain substances affecting the central nerve system, poisons or powerful drugs;
14.Inappropriate testing specifications or data references;
15.Failing to collect licenses or proceed with drug testing within the specified deadline; or the drug testing results fail the assessment due to discrepancy between the results and the data submitted for the application or due to other reasons;
16.Failing to produce, change or modify the product packaging, labels or package inserts in accordance with the approved items; and
17.Any other situations not in compliance with the Regulations, related regulations, or announcements made by the central health competent authority.

Article 26

In situations where fees have not been paid, application forms not submitted, data insufficient or other matters not in accordance with the Regulations, the applicant should take corrective actions before the deadline specified by the central health competent authority. A two-month period is given for correction.
If the applicant is not able to meet the deadline, a written statement should be submitted to support the application of an extension. The extended deadline is one

month after the expiry date of the original correction period. Only one extension will be allowed.

If the applicant fails to make correction within the original or the extended deadline, then the central health competent authority can reject the application based on the currently available information.

Article 27

Upon the receipt of the notice of license collection, apart from proceeding with drug testing, the applicant should pay the fees within the deadline for license collection. The procedure for license collection is as follows:

1.Two copies each of drug labels, package inserts and packaging materials that are printed in accordance with the approved draft should be provided. For new drugs, three copies each should be provided. For imported drugs, properly printed Chinese package inserts, stickers, and the final retailing packaging should be provided;

2.The notification letter stamped with the applicant's official seal and the signet of managing director;

3.The approved draft copy of labels, package inserts and outer packaging that were attached to the license collecting notice should be returned.

4.The photocopy of the application form of drug registration that was attached to the license collecting notice should be returned.

5.A photocopy of drug license that was attached to the license collecting notice should be returned.

License should be collected within three months of the notice date. If the applicant is requested to make corrections due to mistakes in the information on the labels, package inserts, packaging or other related materials required for license collection, the applicant should make corrections within the deadline specified by the central health competent authority before the license can be collected.

Except for the reissuance of damaged or lost drug licenses, all approved post-approval changes will be certified by the central health competent authority through noting down the changes on the original drug license with date and official stamps, then returned to the license holder. Fees for the reissuance of a new license copy will be charged.

After the license was collected, if the applicant does not follow related regulations to proceed with drug testing, or the test results are not in accordance with the contents of the application or are disqualified for some reasons, then the license has to be returned according to the central health competent authority's notice.

Article 28

Upon receipt of a drug testing notice, the applicant should pay the test fees and send the following samples and information to the central health competent authority for

testing before the deadline specified in the notice:
1.Three portions of drug samples. Each portion should be quantity sufficient for carrying out specification analysis for all items;
2.Appropriate quantity of reference standards, if they are needed for the test;
3.Form for sample delivery for drug testing;
4.Fee schedule for drug testing charged by the central health competent authority;
5.Color photos or scanned images of drug samples.
For applications of drug registration or post-approval changes filed during the pharmacovigilance period, if the central health competent authority has concerns regarding quality or other issues, then the following procedures should be taken:
1.If the submitted dossiers are complete, the central health competent authority will inform the applicant to send samples for testing.
2.If the sample passes the tests, but the Bioequivalence (BE) test report or clinical trial report has not yet been reviewed, the central health competent authority shall issue a notice, conceal the data submitted for drug registration in a sealed envelope and return it to the applicant. The applicant should keep the envelope safe and should not open it without permission. If the sample fails the test, punishment will be given pursuant to the Act.
3.After being informed by the central health competent authority of the approval of BE test report or clinical trial report, the applicant should return the sealed envelope along with a photocopy of the notice to the central health competent authority to proceed with the application.
Cases or re-testing will be charged testing fees again.
Article 29
In situations where the applicant proceeds with drug testing prior to the acquirement of license, if the dossiers later fail the review, the applicant shall not request for a refund or return of drug samples.
In situations where the applicant receives a drug license and starts selling the products before the applicant proceeds with drug testing or before the test results are through, the applicant should make an exact list of the manufacturing dates, batch numbers, trading parties and quantities for each batch of products. The list should be submitted to the central health competent authority and local health authorities at 10-day intervals.
In the above-mentioned situations, if the applicant does not comply with related regulations to proceed with drug testing or if the test results are not in accordance with the contents of the applications or for any other reasons it fails the assessment; then, upon receipt of the notice, the applicant should stop manufacturing the products involved and return the drug license immediately. The applicants shall be

punished according to the Act.

Article 30

For the application for drug registration of imported drugs, the regulation of testing samples, their quantity and custom clearance procedure are as follows:

1.In principle, the quantities of samples of testing drugs and reference standards for custom clearance should be consistent with the quantities stated on the letter of notice issued by the central health competent authority. However, to have the packaging remain intact, the applicant may request the custom office to deliberate over the factual packaging and release one single complete package.

2.Manufacturers should follow the Regulations Governing Controlled Drugs and the corresponding implementation rules in compliance with the central health competent authority for approval of the importation and exportation of controlled drugs (including the importation of active pharmaceutical ingredients of controlled drugs for trial manufacturing). This requirement also applies to drugs not classified as controlled drugs in Taiwan but an importation permit is required by the manufacturing country.

The above regulations for testing samples and their quantities and custom clearance procedures are also applied to the applications of post-approval changes of imported drugs.

Article 31

The following procedures apply to drugs already granted with licenses but that have failed the efficacy and safety assessment and to drugs whose formulas should be re-evaluated:

1.If an applicant fails yet again in the appeal after submitting clinical data, then the drug license shall not be extended after its expiration.

2.For those formulas subject to re-evaluation, if the clinical data submitted by the license holder fails the assessment, the drug license shall not be extended after its expiration.

3.For formulas failing the original assessment or those subject to re-evaluation, if the clinical data submitted for re-evaluation passes the assessment, then the post-approval changes or extension of the drug license will be approved. However, if the clinical data is incomplete or the applicant did not resubmit data, the drug license shall not be extended after its expiration.

4.For formulas failing the assessment or those subject to re-evaluation, licenses in relation to the drugs are still valid during the appeal period or before the resubmission of data for re-evaluation. However, if manufacturers do not make appeals or resubmit data, the licenses in relation to the drugs shall not be extended after its expiration.

Section 2 Drug Review and Registration

Article 32

When applying for drug registration, the applicant should provide photocopies of documents to justify that the hardware, software and dosage form equipment of the manufacturers comply with the GMP Guidelines. For toll-manufactured products, the paperwork should include all manufacturers involved in every step of the manufacturing process.

Active ingredients of drug products shall comply with GMP Guidelines.

Article 33

After a drug license was revoked or cancelled due to drug efficacy or safety reasons, the first application of drug with identical active ingredient, dosage form and contents should follow the regulations for the new drug registration. If the reasons for license revocation or cancelation are irrelevant to drug efficacy or safety issues, then the first application shall follow the regulations of generic drugs.

Article 34

If more than four applications for drug registration are to be filed in the same month, the applicant should apply for an approval by giving reasons and providing information on the manufacturer, including information on the equipment and technical staffs of the manufacturing and quality control departments and the manufacturer's actual manufacturing capacity. This information has to be confirmed by the central health competent authority through dossier review or site inspection of quality control, production records, sample manufacturing processes and on-site supervision.

For manufacturers meeting the validation requirements in accordance with the schedule stipulated in Article 21 Paragraph 3, each manufacturer can file three applications for drug registration every month or 36 cases every year.

Article 35

For the application for drug registration of pharmaceutical preparations, the dosage form should comply with the following regulations:

1.If a drug has two different dosage forms, then separate applications should be made. If there are different unit strengths or concentration levels of the same dosage form, then separate applications are required.

2.For powders for injection, different content volumes can be put in one application; but, injections with different concentration levels should have separate applications.

3.Powders for injection with different solvents for muscular injection and for intravenous injection should have separate applications.

4.Manufacturers shall not apply for the registration of a dosage form that has not yet passed the central health competent authority's assessment. However,

manufacturers with the approval of ointment may apply for the registration of drugs in the dosage form of cream or gel. Manufacturers with approval for the sugar-coated tablet and/or the film-coated tablet may apply for the registration of drugs in the dosage form of tablet, granule for internal use and powder for internal use. Manufacturers with approval of tablest may apply for the registration of drugs in the dosage form of granule for internal use and powder for internal use.

Article 36

The Stability study, in support of the application for drug registration should comply with the following regulations:

1.The stability study should include research on the drug degradation curve in order to estimate the period of efficacy and to ensure the effectiveness and safety of drugs in use. The study should be conducted in accordance with the Guidelines on the Drug Stability Study as announced by the central health competent authority.

2.A stability study protocol and a report should be submitted.

3.In order to ensure the sufficiency and completeness of a stability study, the applicant should provide any supplementary or necessary information upon the central health competent authority's request. However, the applicant may retain the original data of a stability study for future inspection. No submission of such data is required.

4.In principle, the stability study of toll-manufactured drugs should be conducted to ensure drug quality. It can be conducted by (but not limited to) manufacturers involved in the toll-manufacturing process.

Article 37

In situations where Bioavailability/Bioequivalence (BA/BE) studies are required for the application for drug registration, the study should comply with the Guidelines on BA/BE Studies in the aspects of the scope of drugs, items, referen ce standards, test principles, test period, principles for substitution and other matters in relation to the study.

When conducting BA/BE studies, the applicant should comply with the central health competent authority's regulation and fill out the application forms for the assessment of the BE study protocol and BE study report, the application forms for the assessment of the BA study protocol and BA study report, and for the assessment of the drug dissolution curve comparison report. The applicant should also prepare related information according to the requirements on those forms.

Article 38

The FSC from the country of origin and the CPP are not required for the application of NCE (New Chemical Entity) drugs.

In cases where the FSC from the country of origin and CPP are submitted for the

aforementioned application, the central health competent authority may adjust the review process according to the actual situation.
For applications of new therapeutic compound, new administration route, new dosage form, new dose or new strength, FSC from the country of origin has to be submitted prior to license acquirement.
If the country of origin is a member of the A10 countries, then the submission of the FSC from the country of origin also satisfies the submission of CPP. If the CPP submitted by the applicant states the same manufacturer's name, address, formulation, dosage form and contents as the information of the new drug in the application, then the submission of CPP also satisfies the requirement of submission of the FSC from the country of origin.
Article 38-1
Apart from the compliance with Article 39, the following dossiers are required for the submission of an NCE drug application:
1.Dossiers of Phase I clinical trial conducted during the development stage in Taiwan, as well as Phase III pivotal trial conducted simultaneously with other countries; or alternatively, Phase II clinical trial and Phase III pivotal trial conducted simultaneously with other countries.
2.A Post-Approval Risk Management Plan; and
3.Relevant documents and information for site inspection upon the central health competent authority's request.
The trial results said in point 1 above have to be approved by the central health competent authority and the design of the trials has to meet the following criteria:
(1)In principle, there should be at least 10 valid Taiwanese subjects for a Phase I clinical trial, such as PK study or PD study;
(2)In principle, there should be at least 20 valid Taiwanese subjects for a phase II clinical trial;
(3)In principle, there should be at least 80 valid Taiwanese subjects for a Phase III pivotal trial; and the results have to show the similarity between Taiwan and other countries; and
(4)With the central health competent authority's approval, the numbers of trials and subjects of the aforementioned three types of clinical trials can be adjusted on grounds of the improvement in quality, safety or efficacy of the drug, the nation's welfare or special circumstances.
Article 38-2
Apart from the compliance with Article 39, applicants of NCE drugs should submit a CPP issued by any one of the A10 countries, plus the dossiers of clinical trials to clinically and statistically justify drug safety and effectiveness in the population in

Taiwan. The results of these clinical trials have to be reviewed and approved by the central health competent authority. If necessary, the central health competent authority may request the submission of post-approval risk management plan.
The aforementioned clinical trials have to meet the following criteria:
1.In principle, there should be at least 10 valid subjects for a Phase I clinical trial, such as PK (Pharmacokinetics) study or PD (Pharmacodynamics) study, conducted in Taiwan.
2.In principle, the number of valid Taiwanese subjects in a multi-national and multi-center Phase II clinical trial should be at least 20 or more than 10% of the total subjects.
3.In principle, the number of valid Taiwanese subjects in a multi-national and multi-center Phase III clinical trial should be at least 80 or more than 10% of the total subjects.
4.For a multi-national and multi- center Phase III study involving any A10 countries and the trial result is going to be used to support the NDA filed to the US FDA or the EU EMA, one of the following conditions has to be met:
(1)In principle, the number of valid Taiwanese subjects should be at least 30 or 5% of the total subjects in a single trial of over 200 (inclusive) subjects; or
(2)In principle, there should be at least10 valid Taiwanese subjects in a single trail of less than 200 subjects.
5.With the central health competent authority's approval, the numbers of trials and subjects of the aforementioned four types of clinical trials can be adjusted on grounds of the improvement in quality, safety or efficacy of the drug, the nation's welfare or special circumstances.
Article 38-3
With the approval from the central health competent authority, clinical trials in compliance with the regulations set out in the previous two articles can be qualified for an exemption of, or a substitution for bridging studies.
Article 38-4
NCE drug applications with the submission of two or more CPPs issued by the A10 countries should comply with regulations set out in Article 39 and 22-1. If necessary, the central health competent authority may request the submission of a Post-Approval Risk Management Plan.
Article 39
Information that should be submitted for the application for drug registration of new drugs, new dosage forms, new administration doses or new unit strength are as specified in Appendices 2 and 3.
Regulations for new drugs stipulated in this Chapter are also applicable to

pharmaceutical preparations with new dosage forms, new administration doses and new unit strengths.
Appendix 2.PDF
Appendix 2.doc
Appendix 3.PDF
Appendix 3.doc
Article 40
Information that should be submitted with the application for drug registration of generic drugs are as specified in Appendices 4 and 5.
Appendix 4.pdf
Appendix 5.PDF
Appendix 5.doc
Article 41
Information that should be submitted with the application for drug registration of bio-pharmaceutical drugs are as specified in Appendices 6 and 7.
Appendix 6.PDF
Appendix 6.doc
Appendix 7.PDF
Appendix 7.doc
Article 42
Information that should be submitted with the application for drug registration of active pharmaceutical ingredients are as specified in Appendices 8 and 9.
Appendix 8.PDF
Appendix 8.doc
Appendix 9.PDF
Appendix 9.doc
Article 43
Information that should be submitted with the application for drug registration of radiopharmaceutical drugs are as specified in Appendices 10 and 11.
The application should comply with the Guidelines on Clinical Trials of Radiopharmaceutical Drugs and the Guidelines on the Assessment of Radiopharmaceutical Drugs as announced by the central health competent authority.
Regulations for new drugs stipulated in this Chapter are also applicable to radiopharmaceutical drugs with new dosage forms and new doses.
Appendix 10.PDF
Appendix 10.doc
Appendix 11.PDF
Appendix 11.doc

Article 44

When applying for licenses for export products, the applicant sh

Section 3 Post-Approval Changes

Article 45

The stability studies, required for the application of post-approval changes, should comply with the following regulations of execution and data submission:

1.For any changes in drugs subject to the submission of the stability study report, the applicant needs to conduct 6-month accelerated stability studies on a batch of changed products, as well as a long-term stability study that tests through the expiration date. Data of at least 3-month accelerated stability studies should be submitted when applying for post-approval changes. The manufacturer should retain the documentation of operational details and test figures of other accelerated studies and long-term studies.

2.For changes in drug expiration date, manufacturers should conduct long-term stability studies on 3 marketed batches of drugs that tests through the expiration date, and analyze the results. For drugs applied for registration before 1 January 2001, manufacturers can decide whether to conduct storage tests or long-term tests based on the Guidelines on Stability Studies. Manufacturers should retain historical documentations of the operational details and original testing results and other related data for inspection; however the applications for post-approval expiration date changes would not be required.

For the documents that should be retained by manufacturers as mentioned above, the applicant has the obligation to provide relevant information upon the central health competent authority's request. If the authority finds any discrepancy in the information, the applicant has to recall all products from the market and receive punishment according to the related regulations in the Act.

Article 46

BA/ BE studies required by the application of post-approval changes should be conducted in compliance with the following regulations:

1. Definitions of major changes and minor changes are as announced by the central health competent authority.

2. The following information should be provided for changes in manufacturing of drugs:

(1) For major changes: BE test reports should be submitted;

(2) For minor changes: a drug dissolution curve comparison report should be submitted.

3. The following information should be provided for changes of the manufacturing site of drugs:

(1) A comparison between formulation and the manufacturing process, including raw material sources, specifications and manufacturing equipment;
(2) A drug dissolution curve comparison;
(3) If according to the assessment, a major change is classified or more information is needed, then the BE test report should be submitted.
4. If the application of post-approval changes involves multiple changes in the formula and manufacturing processes, then regulations corresponding to each change item should be complied.
5. BE tests can be substituted by BA tests along with clinical trial reports.
6. BA/ BE tests should be conducted in compliance with the Regulations for Bioavailability and Bioequivalence Studies
For drugs already approved on the market, if the manufacturer, of their own accord, carried out a BE test and the report has been approved by the central health competent authority, then afterwards, any changes involved in manufacture and manufacturing sites are subject to the regulations in the preceding paragraph.
Article 47
Applications of post-approval changes of imported drugs should provide a notice of changes issued by the original manufacturer. The notice should be issued by the registered original manufacturer or its headquarters, or authorized license holders in other countries; and the notice should be within its one-year validity. The manufacturer's name and address stated on the notice should be identical to those on the approval. The notice should not be issued by affiliates, agencies or distributors or in the form of telegram, price quotation statement, or electronic media.
Article 48
In any of the following situations, manufacturers may, of their own accord, change package inserts, labels, or packaging. However, these changes have to comply with the GMP Guidelines; and the relevant modified operational procedures shall be documented accordingly. Records shall be retained for future inspection. Notification of the post-approval changes in package inserts, labels, and packaging may be declared electronically the approval. Products on the market shall be handled according to the relevant regulations.
1. No changes in the originally approved text:
(1) Only changing the graphic design or colors of labels, package inserts, or outer boxes. The graphic design may not be offensive, indecent, or misleading;
(2) Resizing the approved graphic design or text to fit a different size of packaging, or repositioning the approved graphic design or text;
(3) Changing the fonts of the approved text. However, the font size of English text may not be larger than that of Chinese text;

(4) Changing or adding the corporate identification system (CIS) or anti-counterfeiting labels;
(5) Adding printings on outer boxes or using new outer boxes to replace the labels. The design of text and graphs shall be identical to those approved; or
(6) If an injection is available in different doses, the graphic design and the text on the labels and the outer packaging can be presented in different colors for differentiation.
2. Changes in text without affecting drug quality or medication safety:
(1) Only adding or changing bar-codes, National Health Insurance (NHI) codes, ID codes, “GMP” before the manufacturer’s name, copyright registration number or company trademark approved by the competent authority, trademark registration number, or patent number;
(2) Adding or changing the anti-counterfeiting hotline. Adding or changing the suggested retail price or customer service telephone line of medicines designated by physicians, pharmacists and/or assistant pharmacists, and over-the-counter drugs;
(3) Changing the drug company’s name, the manufacturer’s name or address, or excipients as approved by the central competent health authority, or adding or changing the telephone number, fax number and contact;
(4) Adding or changing the distributor’s name or address. The font size of the distributor’s name may not be larger than that of the license holder’s name. Distributors have to be a qualified pharmaceutical agent;
(5) Adding seal labels (outer boxes) or the changing labels (including price labels);
(6) Adding items on the labels or package inserts of export products upon the request of importing countries;
(7) Adding notes on the approved packaging to indicate that the product is exclusively for the use of certain hospitals or for inpatient use, including other appropriate terms such as “not for resale”;
(8) Adding, deleting, or changing the manufacturer’s name added to the name of the product in English;
(9) Changing the measurement unit of formulas in order to comply with the Chinese Pharmacopoeia;
(10) Changing the terms used in describing the storage conditions without altering the original requirements. The usage of the phrases shall be consistent with the Chinese Pharmacopoeia.
3. Changes in the text of the methods of administration in order to ensure drug quality and medication safety.
The adjustment of the manufactiring date and/or expiry date format of Article 20 paragraph 1 item 18, is not a label or packaging label change.

Article 49

For drugs with licenses and categorized as medicines designated by physicians, pharmacists and/or assistant pharmacists or in the category subject to the Guidelines on the Review of medicines designated by physicians, pharmacists and/or assistant pharmacists, the central competent health authority's announcements shall be followed. Missing the deadlines shall be punished according to the relevant regulations in the Act.

Article 49-1

For active pharmaceutical ingredients or active pharmaceutical ingredients of drug products with licenses, the data involving the changes of technical documents shall be submitted in accordance with Appendix 12.

When applying for addition or change of the source of active pharmaceutical ingredients of the drug products, the following documents shall be submitted:

1. Application form for post-approval changes;
2. Original drug license;
3. A GMP compliance certificate for the active pharmaceutical ingredients newly added or changed;
4. The approvals of the technical documents of the active pharmaceutical ingredients issued by the central competent health authority. However, the technical documents of active pharmaceutical ingredients can be substituted by other dossiers as promulgated by the central competent health authority.
5. Description of the differences in specification between the new and old source of active pharmaceutical ingredient and the evidence;
6. Comparison and evaluation data of the finished preparations according to the characteristics of the dosage forms;
7. If the results compared according to the preceding paragraph are inconsistent, a dissolution test shall be conducted. If the comparison results of dissolution curves are dissimilar ($f2<50$), a drug BE test report shall be submitted.

Appendix 12.PDF

Appendix 12.doc

Article 50

The following documents are required for the application of changes in the Chinese or English product name.

1.Application form of post-approval changes;
2.The original copy of drug license;
3.An assurance statement (A) should be submitted to certify the changes in the Chinese or English product names of a locally manufactured drug, or the change in the Chinese product name of an imported drug. If available, a photocopy of the

trademark registration certificate or approval letter issued by the Bureau of Intellectual Property of the Ministry of Economic Affairs (MOEA) should be submitted; and

4.The application of the change in the English product name of an imported drug should be accompanied with a notification letter of post-approval changes issued by the original manufacturer and the CPP from the manufacturing country.

Article 51

The following documents are required for the application of changes in drug categorization:

1.Application form of post-approval changes;

2.The original copy of drug license;

3.The safety test, clinical references and the pharmacopoeia or formularies of the A10 countries; and

4.A notification letter of post-approval changes issued by the original manufacturer for imported drugs

If the change in drug category is ordered by the central health competent authority based on an assessment result, then Items 3 and 4 in the preceding paragraph can be exempt.

If a license reissue is required, the original copy of the application form for drug registration should be provided.

Article 52

The change of dosage form is restricted to changes among tablets, sugar-coated tablets and film-coated tablets; between cream and ointment or among gel, cream and ointment for external use provided that drugs with identical ingredients, dosage form and dose have been approved by the central health competent authority.

The following documents are required for the change of dosage forms:

1.Application form for post-approval changes;

2.The original copy of drug license;

3.Manufacturing and Control Standard, or the batch records of the same lot as the finished products;

4.Stability study results;

5.For locally manufactured drugs, the testing specifications, methods and certificate of analysis of the finished products, as well as the assurance statement (A) and supporting documents of factory registration;

6.For imported drugs, the testing specifications, methods and certificate of analysis of the finished products and active substances used for the batch, as well as a notification letter of post-approval changes issued by the original manufacturer and the CPP issued by the country of origin are needed.

Article 53

No active pharmaceutical ingredients can arbitrarily be changed. Re-application for drug registration is required for such changes. In any of the following situations, the application of post-approval changes can be filed:

1. Adding declaration of salt forms in vitamin preparations, if those salts are not listed on the license;
2. Changing the measurement units of the antibiotic preparations from weight to potency;
3. Modification is required according to the central competent health authority's concerns over safety or ban on certain ingredients in the formula;
4. Imported drugs certified by the supreme competent health authority of the country of origin wherein the formula change is necessary. The manufacturing methods, testing methods, specifications, stability, or drug re-evaluation reports from the original manufacturer shall be submitted.

The following documents are required for the application of changes of formula.

1. Application form for post-approval changes;
2. Original drug license;
3. Standard Manufacturing and Control Procedures or the batch record of the same lot as the finished product;
4. Data on the stability test;
5. Declaration (A);
6. For locally manufactured drug products, the testing specifications, testing methods, and certificates of analysis for the finished products;
7. For imported drugs, the testing specifications, testing methods, certificates of analysis for the finished products and the raw materials of the same lot as the finished products, a notification letter of post-approval changes issued by the original manufacturer, and CPP from the manufacturing country.

In any of the following situations, reapplication of drug registration is required, but it is not applicable to post-approval change.

1. Same active pharmaceutical ingredients with different doses;
2. The original manufacturer no longer manufactures the originally approved drug product, which is to be replaced by a new preparation whose product name and formula are different from those of the approved drug.

Article 54

The following documents are required for changes in indications:

1.Application form for post-approval changes;
2.The original copy of drug license;
3.Two copies of detailed clinical references of the claimed indications;

4.For locally manufactured drugs, an official reference book recording the new indications is needed. For imported drugs, approval of new indications issued by the central health competent authority of the country of origin and authenticated by the R.O.C foreign affairs offices is needed. If these documents are not available at the time of filing, the applicant shall provide the required documents before approval. The authentication requirement is waived for documents issued by A10 countries;
5.An original approved copy of the form with labels and package inserts attatched along with the central health competent authority's stamp on the seams;
6.Two actual packaging materials (or color photos) or drafts of package inserts, labels, outer boxes, and aluminium blister foil sheets. For imported drugs, two copies of package inserts in the original foreign language are needed;
7.For imported drugs, the notification letter of post-approval changes issued by the original manufacturer is needed.
If there is evidence from clinical trials conducted in Taiwan to justify that the drug is effective and safe for the new indication, then the first applicant applying for the addition of the new indication can be exempt from the requirement described in Item 4 in the preceding paragraph.
The first applicant of the addition of a new indication (including changes of indications and addition of indications) may decide whether or not to conduct local clinical trials. If a local clinical trial has been conducted by the first applicant to justify the drug is effective and safe for the new indication, then during the following 5 years, other applications filed by other manufacturers of drugs with the same ingredients, dosage form and dose, either for licensing the new indication or for extending an existing license, should also provide local clinical trial reports up to the standard conducted by the first successful applicant in addition to all the required documents set out in Paragraph 1 Item 1, 2 and 5-7.
If the first successful applicant of a new indication (including changes of indications and addition of indications) did not conduct local clinical trials; or the approval was issued more than 5 years ago, then any other applications of drugs with the same ingredients, dosage form and dose, either for licensing the new indication or for adding the new indication to an existing license, should provide all the required documents set out in Paragraph 1 Item 1, 2 and 5-7.
If labels and package inserts are revised according to the indications announced by the central health competent authority, the license holder should submit the application form for post-approval changes and the original copy of drug license when applying for post-approval changes of indications.
Article 55
The following documents are required for the changes in drug administration and

dosage:
1.Application form for post-approval changes;
2.Photocopy of drug license (front and back sides);
3.Two copies of detailed clinical references about the claimed drug administration and dosage;
4.An original approved copy of the form with labels and package inserts attatched along with the central health competent authority's stamp on the seams;
5.Two actual packaging materials (or color photos) or drafts of Chinese package inserts, labels, outer boxes, and aluminium blister foil sheets. For imported drugs, two copies of package inserts in the original foreign language are needed;
6.A photocopy of official reference books, or certificates claiming drug dosage and administration approved by the central health competent authority and authenticated by the R.O.C. foreign affairs offices is needed. If these documents are not available at the time for filing, the applicant shall provide the required documents before approval. The authentication requirement is waived for documents issued by A10 countries;
7.For imported drugs, a notification letter of post-approval changes issued by the original manufacturer;
8.A comparison table of the dosage and administration before and after the change.
Article 56
The following documents are required for the change in excipients:
1.Application form for post-approval changes;
2.If the change in excipients could affect the characteristics of the drug, the applicant should follow the notice issued by the central health competent authority to perform drug testing and to provide two copies each of the testing specifications, methods, and certificate of analysis, as well as one copy each of the safety data, BE test data and stability test data;
3.Photocopy of the drug license;
4.For imported drugs, a notification letter of post-approval changes issued by the original manufacturer and the CPP from the country of origin.
For pharmaceutical preparations that already have BE test results, the application of the above-mentioned changes has to comply with Article 46.
Whereas the active ingredients, dosage form, dose and administration route of a licensed drug remain unchanged, the appearances or shapes are altered by changing its aromatics, coloring agents or flavours without any pharmacological effects, and do not affect drug quality or medication safety, then it can be justified by applying for post-approval changes for excipients as the addition of new contents. Appropriate descriptions should be given on labels, package inserts and outer packaging for clear

differentiation. Graphic designs and colors may be changed to suit the new descriptions.

Article 57

The following documents are required for changes of drug testing specifications, methods and product appearance:

1.Application form for post-approval changes;

2.Photocopy of drug license (front and back sides);

3.Two copies each of the testing specifications, methods and certificate of analysis of changed drugs, and an explanation of the differences in specifications before and after the changes;

4.For imported drugs, a notification letter of post-approval changes issued by the original manufacturer.

If the changes of testing specifications and methods are according to the update on pharmacopoeias, then the application form should include details of the cited pharmacopoeias, including the title, publication year, edition and page numbers. The cited pharmacopoeias are restricted to Chinese Pharmacopoeia and pharmacopoeias published in the A10 countries or acknowledged by the central health competent authority and should be within 5 years from the date of publication, the submission of documents mentioned in Item 3 of the previous paragraph can then be exempt. However, manufacturers should retain all original data and figures for future inspection.

Article 58

The following documents are required for changes of immediate packaging materials:

1.Application form for post-approval changes;

2.Original copy of drug license;

3.The Stability study report

4.For injections, the testing specifications, methods and certificate of analysis of finished products. For injections packed in syringes or soft bags, the testing specifications, methods and certificate of analysis of containers;

5.For locally manufactured injections, a photocopy of formulation basis. If the formulation basis is not available, the applicant should provide the safety data of packaging and go through the testing procedure as requested by the central health competent authority.

6.For imported drugs, a notification letter of post-approval changes issued by the original manufacturer;

7.If soft bags are added as a new packaging material of injections, Manufacturing and Control Standard or batch records of the same lot as the finished products should be submitted.

Article 59

The following documents are required for changes in the filling quantity of injections (under conditions of no changes in unit strength and container materials):

1.Application form for post-approval changes;

2.Original copy of drug license;

3.For locally manufactured drugs, a photocopy of the reference of drug administration and dosage; for imported drugs, a notification letter of post-approval changes issued by the original manufacturer;

4.The stability study data in situation where the filling quantity is reduced.

Article 60

The following documents are required for changes in the pharmaceutical company's name without transfer of rights:

1.Application form for post-approval changes;

2.Original copy of drug license;

3.A list of all drug licenses;

4.A photocopy of the changed drug company licenses. No supporting documents of factory registration are required when the complete manufacturing process is commissioned to toll-manufacturers. For imported drugs, the applicant may submit a photocopy of the changed drug company licenses.

When applying for changes mentioned in the preceding paragraph, the applicant can include all drug licenses in one application. If the applicant divides the licenses in different applications, the follow-up applications should quote the document reference number of the first approval or attach a photocopy of the approval letter to the follow-up applications. A photocopy of the drug company's license is not required.

If the merger of multinational companies causes the changes of a drug company's name and the reorganization of different subsidiaries and agents in Taiwan, the application of changes should comply with the following regulations. If the merger involves the transfer of rights, the applications should be jointly filed by both sides.

1.Application form for post-approval changes: The application should be signed jointly by the companies involved in the merger, specifying that the change is due to the merger of multinational companies. However, if the original drug company name is no longer available after the reorganization, then the application can be filed only by the new drug company under the new name;

2.The notification letter of the company merger issued by the foreign manufacturer, its headquarters or the foreign license holder, or officially certified by responsible competent authorities;

3.An original copy of the authorization letter issued by the foreign manufacturer or

its headquarters after the merger, or by the foreign license holder. The authorization letter should be authenticated by the R.O.C. foreign affairs offices;
4.Photocopy of the drug company license after the merger;
5.Assurance statement signed by the person in charge of the drug company after the merger. By signing the statement, the drug company assures that all drugs are imported and sold in compliance with related regulations and the company will take full responsibilities. The company should also make a statement to certify that the manufacturer does not have other products of the same formulation.
6.If prior to the merger, the drug company already held some drug licenses, then the original copies of all drug licenses and a list of all licenses of imported drugs should be attached to the application of changes. In principle, the transfer for all licenses is done in a single application. After the application is approved, the applicant should, of their own accord, change the company's name on all labels, package inserts, outer boxes, aluminium blister foil, etc. Those materials should be submitted upon request for inspection;
7.If prior to the merger the drug company has some drug application cases still in progress, the applicant should fill in another application form (both original and duplicate copies), therein stating the new drug company name.

Article 61

The following documents are required for the application of changes in the drug company name while the address remains the same:
1.Application form for post-approval changes;
2.Original copy of drug license;
3.A list of all drug licenses;
4.For local manufacturers, a photocopy of each changed license;
5.For manufacturers of imported drugs, a notification letter of post-approval changes issued by the original manufacturer and documents certifying the change in the manufacturer's name issued by the highest health competent authority of the country of origin, and authenticated by the R.O.C. foreign affairs offices. The authentication requirement is waived for documents issued by A10 countries.
If the only change is the name of the manufacturer or foreign license holders, while the address remains the same and there is no transfer of rights, the following documents should be submitted for the application of post-approval changes:
1.Application form for post-approval changes;
2.Original copy of drug license;
3.A list of all drug licenses;
4.Notification letter of post-approval changes issued by the original manufacturer.

Article 62

For post-approval change, the following documents are required for the changes of the drug manufacturer's address:

1. If the change is due to building-numbering adjustment, then the following documents shall be submitted:

(1) Application form of post-approval changes;

(2) Original drug licenses;

(3) For local drug manufacturers, a list of all drug licenses, a photocopy of each changed license, and the documents issued by the household registration authorities to prove the implementation of building-numbering adjustment;

(4) For foreign manufacturers of imported drugs, a notification letter of post-approval changes issued by the original manufacturers and documentation issued by the relevant household registration authorities. The documents should be authenticated by the R.O.C. Foreign affairs offices. The authentication requirement is waived for documents issued by A10 countries.

2. The following documents are required for site relocation or changes in the place of production:

(1) Application form of post-approval changes;

(2) Original drug licenses;

(3) For local drug manufacturers, a list of all drug licenses, a photocopy of each changed license, and a photocopy of the GMP certificate for the new site after relocation;

(4) For foreign manufacturers of imported drugs, a letter of proxy, the original notification letter of post-approval changes issued by the original manufacturer, CPP from the manufacturing country, a photocopy of the GMP compliance certificate, the standard manufacturing and control procedures or the manufacturing records of the same lot for the final products, the testing specifications, the testing methods and certificate of analysis for the final products and the raw materials of the same lot, and data of stability tests. If the holder the GMP compliance certificate is not the applicant, then this documentation can be replaced by a letter of authorization issued by the original manufacturer or the local drug company holding the certificate, therein specifying the approval number of the original certificate.

(5) For foreign manufacturers of imported drug substances, a letter of proxy, the original notification letter of post-approval changes issued by the original manufacturer, the GMP compliance certificate of the active pharmaceutical ingredients, and the relevant technical documents as specified in Appendix 12.

(6) For drugs having completed the BA/BE tests, Article 46 should be followed for documentation submission.

(7) If renewal of license is required, the original application form shall be submitted.

For imported drugs, if the foreign manufacturing site's address remains the same, but the address of the drug company or the foreign license holder is changed, and there is no transfer of rights, then the following documents shall be submitted.

1. Application form for post-approval changes;
2. Original drug license;
3. A list of all drug licenses;
4. Notification letter of post-approval changes issued by the original manufacturer.

Article 63

The following documents are required for changes in package inserts, labels, outer boxes and aluminium blister foil or for the reissuance of the originally approved copy that was lost:

1.Application form of post-approval changes;
2.Photocopy of the drug license (front and back sides);
3.Originally approved copy of the form for sticking label and package insert with the central health competent authority's stamp on the seams. Applications of reissuance of the approved copy can be exempt from this submission;
4.Two actual packaging materials (or color photos) or drafts of package inserts, labels, outer boxes, and aluminium blister foil sheets. If there is any change in the package insert, the changes should be highlighted in the draft package inserts, both in Chinese and in foreign language. For imported drugs, the original package inserts and the draft of Chinese translation should be provided. The Chinese version should be precisely translated from the original version. If the changes only occurred in package inserts, then the applicant can just submit package inserts without other packaging materials;
5.For applications of the reissuance of lost original license, an assurance statement should be submitted to certify that the document is missing;
6.A notification letter of post-approval changes issued by original manufacture is required for imported drugs, except for applications of the reissuance of lost license.

Article 64

Applications for registration of pharmaceutical toll-manufacturing shall comply with the Regulations on Pharmaceutical Toll-Manufacturing and Contract Analysis and shall submit the following documents:

1. Application form for toll-manufacturing;
2. A photocopy of toll-manufacturing contracts, therein stating the details about the management of toll-manufacturing;
3. Application form for post-approval changes;
4. Original drug license;
5. A list of all drug licenses categorized by dosage forms, but it is exempted for

toll-manufacturing only one drug license;
6. A description of each toll-manufacturing process. This requirement can be exempted, if a complete manufacturing process is commissioned to the toll-manufacturers;
7. Standard Manufacturing and Control Procedures. This document can be exempted if the local manufacturers have no intention to start the manufacture yet. The certificates should be noted with the phrase: “Manufacturing is not allowed”. Manufacturers are required to submit the Standard Manufacturing and Control Procedures and obtain approval from the central competent health authority prior to production;
8. A photocopy of the contract giver’s company license;
9. A photocopy of each of the contract acceptor’s factory registration license and drug manufacturing permit. For imported drugs, those documents can be replaced with a photocopy of the acceptor’s GMP compliance certificate. If the holder of the GMP compliance certificate is not the applicant, then this document can be replaced by a letter of authorization issued by the original manufacturer or the local drug company who holds the certificate, therein specifying the approval number of the original certificate.
10. The testing specifications and methods of the finished products issued by the contract acceptor;
11. Documents of rescission with previous acceptors. Those entering into a toll-manufacturing contract for the first time can be exempted from this requirement;
12. If the imported drugs were toll-manufactured, a notification letter of post-approval changes issued by the original manufacturer and the CPP from the country of origin shall be submitted. For the imported drug substances, the CPP can be exempt. However, the relevant technical documents for changing toll-manufacture, specified in Appendix 12, are required.
When a BE study of the toll-manufactured drug is completed, documents shall be submitted pursuant to relevant regulations.
The change of the licenses mentioned in Paragraph 1 will be processed by noting the original license rather than issuing another one. However, in situations where the assessment results show that an import permit is required to change into a manufacturing permit, a new license has to be issued. Under such circumstances, the applicant shall complete the checklist for toll-manufacturing dossiers, and provide all relevant documents, as well as the application form for drug registration and the Declaration (A).
After the application is approved, the applicant shall, of their own accord, modify the labels, package inserts, outer boxes, aluminum blister foil, etc. Those materials

should be submitted upon request for inspection.

Article 65

The following documents are required, if the manufacturer intends to manufacture a drug which used to be toll-manufactured.

1.Application letter for the shift from toll-manufacturing to self-manufacturing;

2.Application form for post-approval changes;

3.Original copy of drug license;

4.Original copy of the application form of drug registration;

5.Assurance Statement (A);

6.A photocopy each of the changed certificates and licenses;

7.Manufacturing and Control Standard or batch records of the tentative production batch;

8.The testing specifications, methods and certificate of analysis of the finished products;

9.If the applicant was originally not a GMP manufacturer, then certificate for the GMP compliance should be submitted.

Article 66

Applications for contract analysis should follow the Regulations on Pharmaceutical Toll-Manufacturing and Contract Analysis and provide the following documents:

1.Application letter for contract analysis;

2.Application form for contract analysis;

3.Photocopy of the contract, therein specifying the scope of contract analysis and related issues;

4.The standard operation plan for contract analysis (including sampling method, sample storage method, sample delivery and transfer conditions, etc.) co-established by the appointer and the appointee;

5.Testing specifications and methods of the contracted items.

The central health competent authority may carry out site inspection if it is necessary.

Article 67

Concerning locally manufactured drugs for exportation, the following documents are required for the applications for changes or additions in immediate packaging materials, maximum package size, labels, package inserts, outer boxes, drug names, indications, excipients, testing specifications, methods and appearance:

1.Application form for post-approval changes;

2.Original copy of drug license for the application of changes in drug name, indications, immediate packaging materials and maximum package size;

3.Photocopy of the front and back of drug license for the application of changes or

addition of labels, package inserts, outer boxes, excipients, testing specifications, methods, and product appearance ;
4.Assurance statement for drug exportation;
5.Two copies of the drafts of package inserts, labels, outer boxes and aluminium blister foil for changes of in package inserts, labels, outer boxes and aluminium blister foil;
6.For changes of testing specifications and methods, a description of the differences in specifications before and after the changes. The new testing specifications, methods and certificate of analysis should be retained by the manufacturer for future inspection.

Article 68

The following documents are required for changes in drug storage conditions:
1.Application form for post-approval changes;
2.Photocopy of drug license;
3.The stability study report;
4.For imported drugs, a notification letter of post-approval changes issued by the original manufacturer.

Article 69

The following documents are required for changes in virus strain for a flu vaccine:
1.Application form for post-approval changes;
2.Original copy of the drug license;
3.Two copies of post-change testing specifications, methods and certificate of analysis of the ingredients, manufacturing processes, raw materials and finished products;
4.Drug stability study report. If the stability study report for drugs of the new virus strain is not yet available at the time of application, the applicant can submit the stability study report of the old strain, then submit the report of the new strain when the test is finished;
5.Clinical reference in relation to the new virus strain
6.The originally approved copy of the form for sticking label and package insert;
7.Two copies of the draft of labels, package inserts and outer boxes after the changes;
8.For imported drugs, the notification letter of post-approval changes issued by the original manufacturer and the CPP from the country of origin. A photocopy of the CPP is acceptable when filing the application; but, the original copy has to be submitted before the application can be approved.

Section 4 License Transfer, Renewal and Reissuance

Article 70

The application for transferring a domestic drug license or an imported drug

distributor’s license should be filed by both parties. The following documents should be provided:

1.Application form for post-approval changes signed by both parties;

2.Original copy of the drug license to be transferred;

3.A list of drug licenses to be transferred, therein recording the license number, formula, dose and dosage form;

4.The assurance statement made by the transferee to certify the responsibility. For the transfer of the license of locally manufactured drugs, the assurance statement should also certify the absence of drugs of the same formula;

5.The following documents are required for the application for license transfer of locally manufactured drugs:

(1)Photocopy of the transfer approvals issued by the health competent authorities of the local governments where the transferer and transferee are located;

(2)A list of valid drug licenses held by the transferee, a record of the license number, formula, dose and dosage form;

(3)An assurance statement (A);

(4)A photocopy each of all changed certificates and licenses;

(5)Manufacturing and Control Standard. This document can be exempted, if local manufacturers have no intention to initiate production at present. The certificates should be noted with the phrase: “Manufacturing is prohibited”. Manufacturers have to submit the Manufacturing and Control Standards and obtain an approval from the central health competent authority before production can be started.

6.The following documents are required for the application of imported drug distributor’s license transfer:

(1)A photocopy of the company license of both transferer and transferee;

(2)Original copy of the transfer agreement with signets of both parties;

(3)Original copy of the authorization letter issued by the original manufacturer, stating the termination of the distributing contract with the transferer and the exchange of new contract with the transferee, as well as the addresses of both parties and the drug items involved in the transfer. The authorization letter should be authenticated by the R.O.C. foreign affairs offices;

(4)A statement certifies that the same manufacturer does not have any products of the same formulation as the transferred drug.

When applying for domestic drug license transfer, if the product name on the old license includes a prefix of the transferer’s company name which is not authorized to be used by the transferee, then an application for a change in product name should be filed at the same time. Drugs with BE study data are subject to the Regulations for Bioavailability and Bioequivalence Studies.

Article 71
The following documents are required for the renewal or reissuance of damaged or lost drug licenses:
1.Application form for post-approval changes;
2.A photocopy of drug license (front and back sides). Original drug license is required, if the application is filed due to damages to licenses;
3.Original copy of the application form for drug registration
4.Assurance statement certifying the loss of drug licenses. This document would not be required for cases of damaged licenses.
5.For locally manufactured drugs, one copy each of the originally approved copy of labels and package inserts and two copies of the form for sticking label and package insert. Those whose DOH approval number starts with Wei-Shu-Yeao (Cheng) are exempt from this requirement.
6.For imported drugs, the original copy of an authorization letter issued by the original manufacturer. The letter has to be authenticated by the R.O.C. foreign affairs offices.
Section 5 License Extension
Article 72
Applications for license extension should be filed within six months prior to the expiration date. Applications filed after the deadline will not be processed and the applicants will have to re-apply for drug registration. Those re-applying for drug registration within three months from the expiration of a license are eligible for a simplified procedure as stated in Article 73.
If an application of license extension also involves other post-approval changes, then these applications should be made separately.
If the space on the license for specifying the expiration date is full, the manufacturer can apply for a new copy of license by submitting the original copy of the application form for drug registration.
Article 73
The following documents are required for application for license extension:
1. Original drug license;
2. Application form for drug license extension shall be stamped by the health authority of the local government where the applicant is located. For toll-manufactured products, the application shall be submitted by the license holder and stamped by the health authority of the local government where the license holder is located;
3. For drugs manufactured domestically, supporting documents of GMP compliance certificate and full formula contents shall be provided; for drugs manufactured by

toll-manufacturers, the contract of toll-manufacturing shall also be attached;
4. For imported drugs, the original CPP from the country of origin, the original letter of authorization issued by the original manufacturer and a photocopy of the GMP compliance certificate for the foreign manufacturing site of imported drugs shall be included. If the holder the GMP compliance certificate is not the applicant, then this document can be substituted by a letter of authorization issued by the original manufacturer or the local drug company holding the certificate, therein specifying the approval number of the original certificate. For the imported drug substances, the CPP can be exempted.
5. The supporting documents of the GMP compliance certificate of the active pharmaceutical ingredients.
For application for license extension of imported drugs, if the stability test data have never been submitted to and approved by the central competent health authority, then the stability test data (including documentation of the operation of stability studies and test result data) have to be submitted.
For application for license extension of bio-pharmaceutical products, documents of the testing specifications, methods, and certificates of analysis, and the form of the outer packaging, package insert, and label have to be submitted in duplicate.