สำนักงานคณะกรรมการอาหารและยา
Food and Drug Administration

GUIDELINE ON PROCEDURAL ASPECTS REGARDING MARKETING AUTHORIZATION OF VACCINES IN THAILAND

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GUIDELINE ON PROCEDURAL ASPECTS REGARDING MARKETING AUTHORIZATION OF VACCINES IN THAILAND

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LIST OF ABBREVIATIONS

ACTD	ASEAN Common Technical Document(s)
ASEAN	Association of South East Asian Nations
B.E.	Before Era
BP	British Pharmacopoeia
BPR	Batch Production Record
CPP	Certificate of a Pharmaceutical Product
CTD	Common Technical Document(s)
DNA	Deoxyribonucleic acid
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMOs	Genetically Modified Organisms
GMP	Good Manufacturing Practice
ICH	International Conference on Harmonization
ICH CTD	ICH Common Technical Document(s)
INN	International Non-Proprietary Name
IP	International Pharmacopoeia
MAA	Marketing Authorization Application
MAH	Marketing Authorization Holder
NCL	National Control Laboratory
NF	National Formulary
OSSC	One Stop Service Center
PAR	Public Assessment Report
Ph Eur	European Pharmacopoeia
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PMF	Plasma Master File
PTL	Product Team Leader
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics
TFDA	Thai Food and Drug Administration
TP	Thai Pharmacopoeia
USP	United States Pharmacopoeia
VAMF	Vaccine Antigen Master File
WHO	World Health Organization

GUIDELINE ON PROCEDURAL ASPECTS REGARDING MARKETING AUTHORIZATION OF VACCINES IN THAILAND

1. LEGAL BASIS AND SCOPE

Article 79 of Drug Act B.E.2510 clearly defines that no drug can be manufactured in or imported into the Kingdom of Thailand unless it obtains a marketing authorization from Thai Food and Drug Administration (TFDA).

Article 80, 81 and 82 of Drug Act B.E.2510 respectively identifies the following:

The whole application dossier consisting of quality, non-clinical and clinical information according to the ASEAN Common Technical Documents (ACTD) or ICH CTD for marketing authorization shall be accompanied with the following particulars:

- the application for marketing authorization shall be accompanied with the following particulars:
  -Trade name
  -Formulation
  -Pack size
  -Analytical method
  -Label
  -Product leaflet
  -Other documents as listed in the Ministerial Regulation

- variation of any marketing authorization can not be proceeded unless it obtains prior approval from TFDA

- mechanism to handle the application for marketing authorization and application for variation as well as the issuing of credential certificate for approval of drug registration or variation should be in accordance with Ministerial Regulation No.18 (B.E.2525) by virtue of Drug Act B.E. 2510

Article 10 (1) of Drug Act B.E.2510 clearly defines the duties of Drug Committee to give advice or justification onto the permission of drug to be manufactured, sold or imported into the Kingdom of Thailand and its Marketing Authorization.

In this guideline it is understood that it will involve the procedural aspects regarding marketing authorization of vaccines as defined hereunder.

Vaccine: “A vaccine is an immunogen, the administration of which is intended to stimulate immune system to result in the prevention, amelioration or therapy of any disease or infection. A vaccine may be a live attenuated preparation of bacteria, viruses or parasites, inactivated (killed) whole organisms, living irradiated cells, crude fractions or purified immunogens, including those derived from recombinant DNA in a host cell, conjugates formed by covalent linkage of components, synthetic antigens, polynucleotides (such as the plasmid DNA vaccines), living vectored cells expressing specific heterologous immunogens, or cells pulsed with immunogen. It may also be a combination of vaccines listed above”.

2. ADMINISTRATIVE AND SCIENTIFIC ADVICE

Administrative and scientific advice can be requested during initial development, before an application for marketing authorization or in the post-opinion phase.

3. PROCEDURE FOR SUBMISSION OF THE APPLICATION FOR A TFDA MARKETING AUTHORIZATION DECISION

When preparing the submission of an application for marketing authorization, applicants have the opportunity to meet the TFDA to discuss any procedural, regulatory or legal issues on the proposed submission. Requests for pre-submission meetings should be sent to the TFDA using the "Pre-Submission meeting Request Form".

3.1 Before submission

At least six months prior to submission of an application for Marketing Authorization decision, applicants should notify the TFDA of their intention to submit an application and give a realistic estimate of the month of submission.

In that notification applicants should include:

- a draft SPC;
- an indication on the number of strengths / pharmaceutical forms / pack sizes (if already known);
- if applicable, their intention to present any existing Vaccine Antigen Master File (VAMF) or Plasma Master File (PMF) Certificates
- the details of proposed manufacturing sites for the finished product and active substances
- a specification of any regulatory issues or difficulties already identified which may require clarification or detailed consideration

A member of staff of the Biological Products Section, Drug Control Division, TFDA will be officially appointed as TFDA Product Team Leader (PTL).

The external experts, on whom TFDA can rely when it needs specific expertise, or assessors for the evaluation of applications, are selected in accordance with SOP: P-D2-29

All external experts will be entered in the TFDA' s experts database on the TFDA provision that following completed and signed documents have been submitted to TFDA: (i) Nomination Form, (ii) Public Declaration of Interests and Confidentiality Undertaking Form and (iii) Curriculum Vitae.

In order to ensure standardization of the headings listed in the SPC, the TFDA provides the applicants with a template of what must be included in these documents. This template is available in paper and electronic format, as well as on the TFDA website (http://wwwapp1.fda.moph.go.th/drug/eng/

3.2 Submission of the application

The applicant shall submit the application at the One Stop Service Center (OSSC), TFDA will issue a temporary acknowledgement number to the applicants and within 30 calendar days will complete the validation.

3.3 Dossier to be submitted

The dossier should be submitted in the Common Technical Document format (CTD) either ASEAN CTD (ACTD) or ICHCTD where it is appropriate.

In case the applicant wishes to use existing VAMF or PMF Certificates in the application, the applicant will be required to provide the valid VAMF or PMF Certificate of compliance in accordance with EMEA Directive 2003/63/EC Part III to TFDA and accompanying evaluation reports together with the respective VAMF and PMR data.

In the case of a vaccine containing or consisting of Genetically Modified Organisms (GMO), the application must also be accompanied by the documentation of the competent authorities to the deliberate release into the environment of the GMO.

In addition, applicants must provide evidence of establishment of the applicant in the Kingdom of Thailand and future marketing authorization holder, as well as documents showing their capacity and commitment to perform all the responsibilities required by marketing authorization holder, in particular:

- a document identifying the person for pharmacovigilance who will be the contact person for any specific pharmacovigilance issues, together with a curriculum vitae and contact details

- a document identifying the contact person responsible for any quality issues including its contact details

3.4 Validation by the TFDA

During validation, the TFDA PTL may decide on the need for action relating to matters such as GMP inspection, samples for analysis, GCP inspections, liaison with environmental agencies and completeness of data.

In the event that the TFDA requires additional data, information or clarification in order to complete its validation of the dossier, it will contact the applicant requesting supply of this data, information or clarification within a specific time limit.

3.4.1 Positive outcome of the validation

In case of a positive outcome, within 60 days(1) the TFDA shall notify the applicant in writing that the validation has been successfully completed and request 4 - 7 copies of the dossier to be sent to TFDA external experts by the TFDA PTL. The applicant should also incorporate any additional data or

(1) First Revision January 2009: revised timeline as approved by TFDA

information supplied during the validation phase to the 4 – 7 copies of the dossier. The timetable for evaluation adopted by TFDA will be attached to the letter confirming the positive outcome of the validation. Individual arrangements should be made with the PTL concerning copies in his or her possession.

3.4.2 Negative outcome of the validation

Failure to provide the data, information or clarification requested will result in a negative validation, of which the applicant shall be informed in writing.

If the application cannot be validated the applicant will be invited to either collect the dossier or have it destroyed by the TFDA.

The applicant will be required to initiate a new procedure should a new complete dossier be submitted in the future to the TFDA.

3.4.3 Management of applications

Once validated, details of the product will be entered into the TFDA tracking system. The numbering system allows for a clear identification of any application for the TFDA marketing authorization decision, the variation, the transfer of a TFDA marketing authorization decision for any vaccine and for any of its presentations throughout its life cycle.

Applications for a TFDA marketing authorization decision for a vaccine can be identified by either the invented name, if available, or the international non-proprietary name (INN) / common name of the active substance(s) of the product in combination with the name of the applicant, where appropriate.

However for administrative purposes and in the context of this guideline, each application is also given a core-number composed of four sections: 1A9000X/year , 2A9000X/year, 1B9000X/year, 2B9000X/year, 1C9000X/year, 2C9000X/year, where 1 stands for one active substance, 2 for more than one active substances, A for manufacture, B for repack, and C for import.

3.5 Need for samples and sample analysis

Samples for testing the proposed vaccine are not required at time of submission of the application.

However the TFDA requests the applicants to submit their vaccines for testing of samples of the vaccine and /or its constituents at the Division of Biological, Department of Medical Sciences as early as possible in order to obtain test in due course.

The NCL (Division of Biological, Department of Medical Sciences) in close collaboration with the TFDA will specify a test protocol (type of samples, number of samples, number of batches, testing to be performed and methods and specifications to be used).

The results of the tests are reported to the TFDA PTL for consideration in finalizing the TFDA Assessment Report.

4. PRE-OPINION INSPECTIONS: GMP INSPECTIONS

The legal basis for pre-opinion inspections of manufacturers of vaccines in connection with TFDA marketing authorization decision is laid down in TFA Regulation and SOP P-D3-115 "GMP Assessment in Marketing Authorization Process", which provides that:

"Where it considers it necessary in order to complete its examination of an application, the TFDA Inspectorate Unit may require the applicant to undergo a specific inspection of the manufacturing site of the vaccine concerned. The inspection shall be carried out before the marketing authorization is granted".

Then TFDA has a coordinating role for these inspections whilst the responsibility for carrying them out rests with the TFDA Inspectorate Unit. For applications where the manufacturer of the vaccine is located inside the Kingdom of Thailand, the TFDA Inspectorate expert may be accompanied by staff from Biological Products Section.

For applications where the manufacturer of the vaccine is located outside the Kingdom of Thailand the responsible authority for inspection will be the Competent Authority of the exporting country and / or the Competent Authority where the manufacturing facilities are is located.

4.1 Pre-submission notification by the applicant for a TFDA marketing authorization decision

In their notification of intention to submit, applicants should mention the name (including contact point) and the address of the proposed manufacturer of the active substance(s) and finished product. The sequence of all different sites involved should be clearly described (as a flowchart).

4.2 Designation of an inspection team and preparation for the inspection

Once the application applicant is received, the TFDA determines whether or not the manufacturing and control sites(s) concerned have already been inspected, by whom, and if satisfactory inspection reports from the last 2-3 years are available. Where a satisfactory report is not available, the TFDA contacts the Inspectorate Unit, and a decision is made whether or not to make a request for an inspection in connection with specific aspects of the application and/ or, in the case of manufacturers in third countries, for general GMP compliance.

Each request for inspection must be adopted by the TFDA. Inspections, where requested by the TFDA, should be carried out and finalized before the marketing authorization is granted.

4.3 Contacts with the applicant and the manufacturer(s) to be inspected

Once the TFDA has requested an inspection and the inspection team has been agreed, the TFDA notifies the applicant that an inspection will take place, and gives details of the inspection team.

The inspectors make the arrangements with the manufacturer and set an inspection date. In the preparation of the inspection, the manufacturer(s) or the applicant may be asked to provide information about the site and operations to be inspected.

Prior to the inspection, the PTL liaises with the inspection team on any points for special consideration during the inspection and whether or not any aspect of the manufacture of the starting material(s) is critical to ensure the quality of the finished product, in which case an inspection of the starting material(s) will also be considered.

4.4 Inspection and transmission of the report

At the end of the inspection, the inspectors make a report of the main findings to the management of the site or company inspected.

Inspection reports, in accordance with the PIC/S format, are provided by the inspection team within 30 days of each inspection.

The draft inspection report is sent by the inspectors to the management of the site or company with a request for comments on major factual errors, points of disagreement or remedial actions to be provided within 15 days of receipt. The timing of any discussions or the provision of additional information will be agreed and communicated to the TFDA PTL.

4.5 Submission of the final report to the TFDA PTL

One month after transmission of the inspection report to the manufacturer, the inspection team send their report to the TFDA PTL indicating whether or not the report has been agreed by the company inspected and, if not, the reason. A copy of the comments from the manufacturer is included. In all cases the inspection team will include their final conclusions.

This must be completed before the TFDA marketing authorization is granted.

Any further pre-opinion inspections that are needed are coordinated by the TFDA PTL.

5. PRE-OPINION INSPECTIONS: GCP AND GLP INSPECTIONS

5.1 GCP inspections during the assessment of the application

Inspections to evaluate compliance with Good Clinical Practice (GCP) are conducted by GCP Inspections Working Group of the TFDA.

The application documents must include a statement to the effect that clinical trials carried out outside the Kingdom of Thailand meet the ethical requirements of WHO GCP or ICH GCP.

5.2 Operational Aspects

All new applications are examined to assess the need for GCP inspection(s). The GCP Inspections Working Group of the TFDA will liaise closely with the TFDA PTL, during the pre-submission phase and in the period during and

immediately after validation to discuss the need to request GCP inspection(s). A need for inspection(s) may be identified at this stage, based on previous relevant experience of the GCP Inspections Working Group of the TFDA.

The assessment of the dossier may also identify a need for GCP inspection(s). Inspection(s) may be requested for adoption by TFDA PTL at any stage of the assessment. In general GCP inspection issues are addressed in the consolidated List of Questions. This will allow these GCP inspection related issues to be addressed within the "clock stop" period.

The applicant is requested to provide the information in the Marketing Authorization Application (MAA) in order to facilitate the review of the application and where needed preparation of GCP Inspections. This information should be provided in the individual Clinical Study Reports and their Appendices in line with the relevant ACTD or ICH CTD.

A list of inspection(s), already conducted or planned by other regulatory authorities, relating to the product and trial sites involved, should also be provided, preferably attached to the Application cover letter.

Each clinical study report should contain a statement indicating whether the study was performed in compliance with Good Clinical Practice (GCP), including the archiving of essential documents. A discussion on GCP compliance should also be included in the Clinical Overview.

This information is required at the time of submission or upon request of all new applications and variations where new clinical data is presented.

Sites are expected to be inspection-ready and have relevant documentation, facilities and personnel readily available in the event that an inspection is requested. If an inspection is requested, the applicant will be required to provide the TFDA with a written statement that the sites accept to be inspected and to make available all documents required, including medical records/source data at the investigator sites, for direct access by the inspectors. This commitment will be required prior to the departure of the inspection team on the inspection, in its absence the inspection may not be able to proceed. If data are not available for review by the inspectors they may not be acceptable (as they can not be verified with the source).

5.3 GLP inspections

The assessment of the non-clinical data in the application includes an evaluation of statements provided on GLP compliance, and the scientific content and if considered necessary by the TFDA PTL, an inspection request can be adopted. The inspection will be carried out by the TFDA Inspectorate Unit.

6. SCIENTIFIC EVALUATION OF AN APPLICATION BY THE TFDA

The assessment will be performed according to Pharmacopoeia Monographs such as BP, USP/NF, Ph Eur, IP and TP which are legally binding; in absence of these, or otherwise justified, WHO guidelines apply. Deviation from WHO and other equivalent International Guidelines needs to be justified by the

applicant. The TFDA will decide on the appropriateness of such justifications, taking into account possible adjustments as appropriate (stability).

The evaluation procedure in International cooperation might be envisaged by TFDA.

6.1 Timetable for the evaluation

Once the application is validated with the positive outcome the TFDA PTL starts the procedure.

Having taken into consideration the standard timetable agreed by the TFDA for the evaluation of an application for a TFDA marketing authorization decision, an agreed timetable should be available on TFDA website.

6.1.1 Standard Review

The TFDA shall ensure that the marketing authorization decision is made within 480(1) working days.

6.1.2 Accelerated Review

When a marketing authorization application is submitted for a product of major public health interest, the applicant may request an accelerated/fast track review as laid down in TFDA Regulation, then TFDA shall ensure that the marketing authorization decision is made within 280(1) days.

Standard timetable for the evaluation of an application for a TFDA marketing authorization decision

DAY	***ACTION***
1	Start of the procedure
90***(1)**	The TFDA adopt a list of questions as well as the overall conclusion and review of the scientific data to be sent to the applicant by the TFDA **Clock stop**. At the latest by Day 120(1), adoption by the TFDA of for GMP/GCP inspection, if necessary (Inspection procedure starts).
120*(1)	Submission of the responses, including revised SPC, labeling and package leaflet texts in English and/ or Thai (where required by Drug Act), and restart of the clock.

* target dates for the submission of responses are published on the TFDA website (http://www.fda.moph.go.th/)
(1) First Revision January 2009: revised timeline as approved by TFDA

After receipt of the responses, TFDA will adopt a timetable for the evaluation of the responses. In general the following standard timetable will apply:

DAY	***ACTION***
150(1)	TFDA revised Assessment Report based on responses of the applicant and revised assessment report to external experts for their consideration and comments
210(1)	Deadline for comments from TFDA external experts to be sent to TFDA PTL
300(1)	TFDA will consider the preliminary Assessment Reports from TFDA PTL. From these preliminary Assessment Reports identified the outstanding issues which the applicant should address. A consolidated list of questions, identifying "major objections" and/or "other concerns" may be adopted. These will be sent to the applicant together with the TFDA recommendation and scientific discussion. **The clock will be stopped at this point.** TFDA discussion and decision on the need for an oral explanation by the applicant. If oral explanation is needed, **the clock is stopped** to allow the applicant to prepare the oral explanation. Submission of final inspection report to TFDA PTL by the inspection team (at the latest by Day 420(1)).
301(1)	Restart the clock and oral explanation (if needed).
320(1)	Final draft of English SPC, labeling and package leaflet sent by applicant to the TFDA PTL
By 320(1)	Adoption of TFDA marketing authorization decision

(1) First Revision January 2009: revised timeline as approved by TFDA

After adoption of a TFDA marketing authorization decision and TFDA final Assessment Report, the preparation of the annexes to the TFDA Public Assessment Report (TFDA PAR) on a TFDA marketing authorization decision in cooperation with the external experts are carried out in accordance with the following timetable.

DAY	***ACTION***
By 321(1)	The TFDA forwards its marketing authorization decision and the relevant annexes to the applicant.
By 350(1)	Finalization of TFDA PAR in consultation with TFDA PTL and applicant (the latter for consideration of confidentiality aspects)

(1) Second Revision April 2015: revised timeline as approved by TFDA

6.2 Liaison between the applicant and the TFDA

For general information regarding the procedure, the applicant is advised to liaise with the TFDA PTL. When during the course of the scientific assessment, clarification regarding specific issues relating to the data submitted is necessary, the applicant and the TFDA may liaise directly.

6.3 TFDA' s request for additional information

The TFDA will consider the Assessment Reports from the TFDA PTL. From these Assessment Reports identified the outstanding issues which the applicant should address. A consolidated list of questions, identifying "major objections" and/or "other concerns" may be adopted. These will be sent to the applicant together with the TFDA's recommendation and scientific discussion. The clock will be stopped at this point.

The TFDA recommendation will state whether:

- the vaccine could receive a positive TFDA marketing authorization decision provided satisfactory answers are given to the "other concerns" and the indications, other elements of the SPC or other conditions

- the provisional view of TFDA is that the vaccine is likely to receive a negative TFDA marketing authorization decision since there are "major objections" which have been identified in the detailed List of Questions.

The applicant would normally be expected to respond within the time frame agreed by TFDA, not exceeding 2 months from the date of receiving the questions. If the applicant is unable to respond in the time frame, then careful consideration should be given to withdrawing the application and resubmitting, if necessary after obtaining scientific advice, when the full information is available. The applicant is advised to consult with the TFDA PTL if clarification is required on any of the questions. The applicant may also wish to consult the TFDA PTL regarding the strategy for the response and revision of indications, other elements of the SPC or other conditions for a favourable TFDA marketing authorization decision.

6.4 Oral explanation

In addition to the written responses to the issues raised by TFDA, applicants may also avail themselves of an oral explanation to TFDA Scientific Sub-Committee. The time limit set out in the TFDA Regulation shall be suspended for the time allowed to the applicant to prepare an oral explanation (clock-stop -usually not longer than 2 months).

Applicants may also be invited by TFDA for an oral explanation. The TFDA will discuss the revised Assessment Report and the comments of other external experts on the report. The TFDA may then identify outstanding issues, which the applicant will be asked to address during such oral explanation.

The time for an oral explanation should not exceed 30 minutes.

7. THE FDA MARKETING AUTHORIZATION DECISION

TFDA adopts its marketing authorization decision in the light of the final recommendation of external experts, the TFDA discussions and further evidence presented at the oral explanation. The TFDA in co-ordination with the TFDA PTL, taking account of the full scientific debate within TFDA and the conclusions reached, prepares the final assessment report, which, once adopted by TFDA, becomes the TFDA scientific opinion assessment report and is appended to the TFDA marketing authorization decision. The TFDA scientific opinion assessment report shall contain the conclusions on the Quality, the Safety and Efficacy and will take into account appropriate benefit/risk scenarios on the populations and conditions of use as documented with clinical data by the applicant.

The TFDA marketing authorization decision which may be positive or negative, is, wherever possible, reached by scientific consensus.

7.1 Favourable opinion

In the event of a positive TFDA marketing authorization decision, the following documents must be annexed and/or appended to the scientific opinion.

- An SPC in English;
- Conditions for manufacturing, batch release and supply;
- A draft labeling and package leaflet in Thai and/or English presented in accordance with relevant provisions of Drug Act;
- The TFDA final assessment report.

Should TFDA want to record any post-opinion follow-up, it will be included in the Assessment Report and referenced in an annexed letter of undertaking signed by the applicant.

7.2 Post-opinion follow-up

For all favourable opinions of TFDA, it might be necessary to establish post-opinion follow-up in an agreed timeframe.

Unless otherwise requested by TFDA, the data on the fulfillment of post-opinion follow-up should be sent by the Marketing Authorization Holder (MAH) to the TFDA. The data will be reviewed in accordance with the agreed timetable.

The MAH will be informed of the outcome of TFDA discussions.

Resulting variation applications

MAHs should submit, within an agreed timeframe, any variation application resulting from the fulfillment of post-opinion follow-up.

Non-fulfillment of post-opinion follow-up

MAHs must indicate realistic target dates for the submission of the post-opinion data in their letter of undertaking.

If no documentation is received in order to fulfil the post-opinion follow-up before the dead-line previously agreed by TFDA and after having received reminder letters from the TFDA, the matter will be put by the TFDA on the Agenda of the following TFDA Scientific Sub-Committee Meeting.

In case of non-fulfilment of post-opinion follow-up, TFDA can, after having consulted with TFDA Scientific Sub-Committee, revise its opinion based on the re-assessment of the benefit/risk profile of the vaccine.

7.3 Unfavourable scientific opinions

The TFDA immediately informs the applicant when the opinion of TFDA is that the application does not satisfy the criteria for a positive TFDA marketing authorization decision.

The TFDA scientific assessment report stating the reasons for its negative conclusions shall be annexed to the opinion.

8. STEPS FOLLOWING THE TFDA MARKETING AUTHORIZATION DECISION

8.1 Transmission of the TFDA marketing authorization decision and use of the decision

If within 30 days of receipt of the decision, the applicant does not inform the TFDA of any intention to request a re-examination, the TFDA will then forward the decision (and the required annexes) together with the TFDA assessment report, within 30 days of its adoption to the applicant.

The decision and its annexes are sent by mail.
The current WHO Certification Scheme accommodates the issuing of Certificates of a Pharmaceutical Product (CPP) for products having received a positive TFDA scientific opinion in cooperation with TFDA external experts. The TFDA will issue the CPP upon request from the MAH.

8.2 Request for re–examination

The applicant may notify the TFDA of its intention to request a re-examination within 30 days of receipt of the decision (after which if he does not request a re-examination, he shall be deemed to have agreed with the decision and it becomes final decision).

The grounds for the request for re-examination must be forwarded to the TFDA within 60 days of receipt of the decision. If the applicant wishes to appear before TFDA for an oral explanation, the request should also be sent at this stage.

The TFDA may decide to appoint additional external expert(s) to re-examine the decision. Within 60 days from the receipt of the grounds for the request for reexamination, TFDA will consider whether its decision is to be revised. If considered necessary, an oral explanation can be held within this 60 days timeframe.

Once TFDA issues a final re-examined scientific decision, it is forwarded (with the required annexes and the reasons for its conclusions) within 15 days of its adoption to the applicant.

8.3 Public Assessment Report on the TFDA marketing authorization Decision

For reason of transparency, the TFDA shall make publicly available the TFDA assessment of the vaccine and the reasons for the favourable TFDA scientific

decision, after deletion of any information of a commercially confidential nature.

This document is called the TFDA Public Assessment Report (TFDA PAR) on a marketing authorization decision. Updates to the TFDA marketing authorization decision will be reflected in the TFDA Public Assessment Report.

8.3.1 Operating approach to the preparation of the TFDA PAR

The responsibility of preparing the TFDA PAR rests with the TFDA and will be coordinated by the TFDA PTL. The preparation of the TFDA PAR is required in cases where TFDA formulates positive final decision.

Applicants will receive the assessment report of TFDA. Applicants are then required to identify within a short period of time (for example within 30 days of adoption by TFDA) those issues which they consider to be commercially confidential. Such issues should be notified and justified by the applicant to the TFDA PTL.

Upon receipt of the applicant's response on issues which the applicant considers to be commercially confidential, the TFDA PTL will prepare a draft of the TFDAPAR, taking into account the obligations of the Regulation, transparency and confidential considerations.

8.3.2 Availability of the TFDA PAR

Once TFDA has agreed on the text, the TFDA PAR will be sent to the applicant. The TFDA PAR shall be made available at the TFDA web site after adoption by TFDA.

9. UPDATING THE TFDA MARKETING AUTHORIZATION DECISION

The MAH is responsible to update the TFDA marketing authorization decision with post-opinion follow-up and variations.

10. PHARMACOVIGILANCE

The MAH, by virtue of its contact person for pharmacovigilance, should ensure that:

- a vaccine, for which a positive decision has been granted in accordance with this procedure, is entered in the VIGIBASE
- all serious adverse reactions to a vaccine, for which a positive decision has been granted in accordance with this procedure, are recorded and reported promptly to the TFDA
- detailed records of all suspected adverse reactions are submitted, in the form of a periodic safety update report, to the TFDA immediately upon request or at least every quarter after the first marketing authorization granted by TFDA during the first two year of its conditional marketing authorization approval. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon

request. These reports shall be accompanied by scientific evaluation, particularly of the benefit/risk balance of the vaccine, to be reviewed by the TFDA PTL and external experts

- any other information relevant to the evaluation of the risks and benefits of a vaccine is submitted, particularly information concerning post-authorization safety studies

11. BATCH CONTROL, PRODUCT DEFECTS AND PRODUCT RECALLS

The MAH shall carry out tests on samples of each batch of the vaccine before release on the market, according to the specifications and analytical methods approved by TFDA.

The NCL on behalf of TFDA will perform its own batch release testing and/or review of batch production record (BPR) before the vaccine is officially released onto the market in the Kingdom of Thailand.

The MAH should report to the TFDA where the vaccine is marketed and inform the TFDA about any defect in a vaccine that could result in a recall or abnormal restriction in supply, together with the corrective actions proposed. Product recalls are the responsibility of the manufacturer and the TFDA.

In cases where the quality issues cannot be resolved by the corrective actions to ensure the protection of public health as proposed by the applicant, the TFDA can, after having consulted with TFDA Scientific Sub-Committee, revise its decision.

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5. Proposed Harmonized Requirements for the licensing of Vaccines in the Americas. Guideline for preparation of applications. PANDRH Guidelines version 01/21/03/2008

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6. Guideline on procedural aspects regarding a CHMP scientific opinion in the context of cooperation with the World Health Organization (WHO) for the evaluation of medicinal products intended exclusively for markets outside the community. EMEA/CHMP/5579/04 Rev.1

7. The rules governing medicinal products in the European Union.

8. Notice to Applicants, Volume 2A Procedures for marketing authorisation, Chapter 4, Centralised Procedure, April 2006.

9. Notice to Applicants, Volume 3 Scientific guidelines for medicinal products for human use

10. Notice to Applicants, Volume 4 Guidelines for good manufacturing practices for medicinal products for human use

11. Notice to Applicants, Volume 9 Guidelines for pharmacovigilance for medicinal products for human and veterinary use

12. Notice to Applicants, Volume 10-Guidelines for clinical trial

13. A guideline on summary of product characteristics. October 2005 Revision 1

14. Note for guidance on preclinical pharmacological and toxicological testing of vaccines. CPMP/SWP/465/95

15. Conduct of pharmacovigilance for centrally authorized products. CPMP/183/97

16. Commission Directive 2003/63/EC of 25 June 2003, Part III, pages L159/80 - L159/81.Guideline on requirement for Plasma Master File (PMF) and Vaccine Antigen Maser File (VAMF) certification

17. Human Medicines – CHMP Assessment Reports

Pre-authorisation Assessment Templates and Guidance

http://www.emea.europa.eu/htms/human/chmptemplates/artemplat es.htm

These documents encompass Quality, Non-Clinical and Clinical aspects, giving the format and guidance on what kind of information is expected under the different headings.

Guidance (PDF) Downloads

D80 AR Overview Guidance

D80 AR Quality Guidance

D80 AR Non-Clinical Guidance

D80 AR Clinical Guidance

Template (Word) Downloads

D80 AR Overview Template

D80 AR Quality Template

D80 AR Non-Clinical Template

D80 AR Clinical Template

D80 Questionnaire

D150 JAR Clinical Template

D150 JAR Non-Clinical Template

D150 JAR Quality Template

D150 JAR Overview Template

D180 JAR Clinical Template

D180 JAR Non-Clinical Template

D180 JAR Quality Template

D180 JAR Overview Template

D120 LoQs Template

D180 LoOs Template

ANNEXES

Annex 1: SOP for Recruitment of the FDA's External Experts (SOP P-D2-28)

Annex 2: SOP for Selection the FDA's External Experts for Assessment of the Marketing Authorization Applications of Vaccines (SOP P-D2-29)

Annex 3: SOP Marketing Authorization Process of Vaccines (SOP P-D2-31)

Annex 4: SOP Assessment of Quality Dossiers for MA Applications of Vaccines (SOP P-D2-32)

Annex 5: SOP Assessment of Non-Clinical Dossiers for MA Applications of Vaccines (SOP P-D2-33)

Annex 6: SOP Assessment of Clinical Dossiers for MA Applications of Vaccines (SOP P-D2-34)

Annex 7: SOP Checking of Experts (SOP P-D2-35)

Annex 8: SOP Public Assessment Report of Vaccines (SOP P-D2-36)

Annex 9: SOP Communication and Collaboration with External Experts (SOP P-D2-37)