Regulatory Guide on
The Registration of Synthetic Peptides Human Pharmaceutical Products that refer to a Reference Peptide Product of rDNA Origin

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Introduction

This Regulatory guide is concerned with regulating the rules and procedures of the development, quality specification aspects and registration of Synthetic Peptides that refer to a reference peptide product of rDNA origin as human pharmaceutical products in the Egyptian Drug Authority in accordance with EDA Chairman Decree 450/2023 (Non-Routine Track (B)).

EDA Relies in its assessment on quality, safety and efficacy data of pharmaceutical products registered in one of Stringent Regulatory Authorities included in the list of reference countries approved by the Technical Committee of Drug Control

Scope

This regulatory guide is applied for synthetic peptides pharmaceutical products that refer to a reference peptide product of rDNA origin and not applicable to biological and biotechnological products manufactured by recombinant technologies, radiopharmaceuticals, and radiolabeled products containing peptides

This regulatory guide shall apply to the Synthetic Peptides pharmaceutical products that are manufactured locally in factories inside the Arab Republic of Egypt for the purpose of local marketing or the imported human pharmaceutical products from one of the stringent regulatory authorities (SRAs) included in a list of the reference countries approved by the Technical Committee for Drug Control or the products imported from a non-reference country and marketed in one of the reference countries approved by the Technical Committee for Drug Control.

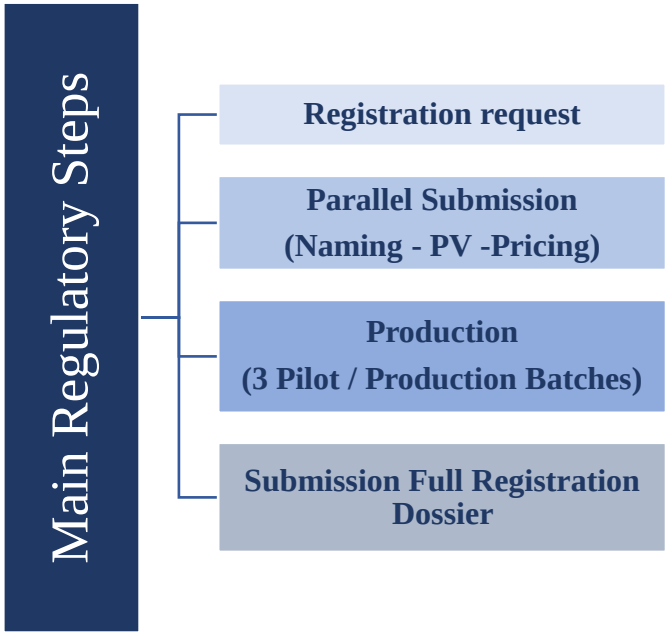
Definitions

- **Synthetic Peptides:** Synthetic peptides are at the interface of small molecules and proteins, they are "Alpha amino acid polymers composed of 40 or fewer amino acids and have challenges in development and manufacture.
- **Orthogonal analytical methods:** methods that use different physical principles to measure the same property of the same sample with the goal of minimizing method-specific biases and interferences
- **EDA Chairman Decree 450/2023:** EDA Chairman decree that regulates the registration process of human pharmaceutical products.

Procedures

The Regulatory Procedures of Synthetic Peptides in accordance with the **Non-Routine Registration track (B) on Decree 450/2023** outlines a series of steps to ensure the safety, quality, and efficacy of the products.

A) The Regulatory Procedures of Synthetic Peptides for locally manufactured human pharmaceutical products:



First: Procedures for obtaining the registration request approval:

- The company is obligated to submit a registration request in accordance with the regulatory mechanisms of the General Administration of Human Pharmaceuticals Registration published on the Egyptian Drug Authority website. This request shall be accepted in accordance with the date and time of its submission in complete and correct form, provided that the company shall receive acceptance of the initial acceptance of the registration request within 3 working days from the date of receiving the completed registration request.
- The company shall be notified of the **status** of the product within a maximum of 18 working days from the date of the initial Acceptance of the fulfilled registration request.

- In the case there are documents required to be fulfilled, the company shall be obligated to complete any required documents within a maximum of 3 months from the date of its notification.
- The registration request approval shall be issued within 10 working days from the date of receiving the fulfilled required documents. The Company shall be obligated to pay the consideration of product registration before heading for receiving the registration request approval, provided that the company shall receive the registration request approval within 30 working days from the date of its issuance, otherwise the registration request will be cancelled**.**

Note:

- The number of registration requests available to be submitted per month shall be **counted** within the submission numbers of the specific registration requests, and in case the company is desirous to submit other registration requests in the same month, the company shall be obligated to **pay** the service consideration prescribed for additional requests other than the number permitted to be submitted per month.
- If the pack of the reference product is a pre-filled pen, it is allowed to use a cartridge instead of a pre-filled pen for the submitted synthetic Peptide product (**In case of company desire**)

Second: The company shall apply in parallel to the following departments:

1. Evaluation Unit for Trade Named and Mock-up of Human Pharmaceuticals

- The company shall submit a list of 15 proposed trade names within a maximum period of 30 working days from the issuance date of the registration request approval, otherwise, the registration request approval will be cancelled based on a report submitted by the relevant central administration.

- Evaluation Unit for Trade Named and Mock-up of Human Pharmaceuticals shall review the list of trade names submitted by the company within 15 working days from the date of receiving the list of names from the company, and naming approval shall be issued to the company, or the rejection notification of the first list of names that are previously submitted.
- In the case of rejection, the company shall be obligated to submit another list within a maximum of 20 working days from the date of rejection of the first list of names that are previously submitted.
- The company shall be permitted to submit a maximum of 4 lists of the proposed names, including the first list of names, provided that the evaluation and approval shall be issued as mentioned above.
- In the case of rejecting the four lists submitted by the company, an approval of the scientific name alongside the company name shall be issued.

2. Central Administration of Pharmaceutical Policies and Market Access /General Administration of Market Access and Business Continuity – Administration of Pricing Policies

- The required documents for pricing shall be submitted within 30 working days from the issuance date of the registration request approval, otherwise, the registration request will be cancelled based on a report submitted by the relevant central administration.
- The product shall be priced within a maximum period of 90 working days from the date of receiving the complete pricing file.

3. Central Administration for Pharmaceutical Care / General Administration of Pharmaceutical Vigilance

The Pharmacovigilance Requirements shall be Submitted within 30 working days from the issuance date of the registration request approval according to the regulatory

mechanism of the General Administration of Pharmaceutical Vigilance, otherwise, the registration request will be canceled based on a report submitted by the relevant central administration. The documents submitted by the company shall be evaluated within a maximum of 60 working days from the date of receiving the fulfilled pharmacovigilance documents (provided that the document describing the Pharmacovigilance system of the company shall be completed upon evaluation).

(a) In case of the approval of General Administration of Pharmaceutical Vigilance:

The company shall be notified of the approval and the product registration procedures shall be completed. In case the company is required to fulfill other documents, the company shall be given a period of a maximum of 30 working days (this period may be renewed for one time, when necessary). The evaluation shall be finished by the General Administration of Pharmaceutical Vigilance within 30 working days from the date of receiving the required documents.

(b) In case of non-approval or non-fulfillment of the documents:

The registration request shall be presented to the Technical Committee for Drug Control by the General Administration of Pharmaceutical Vigilance to take the decision it deems appropriate and to state the reasons in the case of rejecting the registration request.

Third: Manufacturing of the three Pilot/Production batches

- The Production must be done in a maximum period of **12 months** from the registration request approval, otherwise, the registration request approval will firmly be **cancelled** based on the report submitted from head of Central administration of pharmaceutical products to be approved by EDA Chairman, **any request for additional period has not been allowed.**

- The company shall apply to The General Administration for Importation and Customs Release for importing the raw material and packaging materials, according to the regulatory mechanisms along with its continuously updated versions.
- Before production, the company shall apply to the Central Administration of Operations as per the regulatory mechanisms of the relevant central administration for producing the three Pilot/Production batches, in the presence of an inspector from the Central Administration of Operations, provided that the Pilot batches shall never be marketed.
- By virtue of the importation approval concerning the raw materials used in the product, the company shall get acceptance for production in the presence of an inspector from the Central Administration of Operations to ensure that the pilot/production batches are produced on the same production lines located in the factory
- The inspector shall attach the composition according to which the production was made and this composition shall be signed by the factory administration officer and shall be signed and stamped by the inspector.

Fourth: Submission of Full Registration Dossier for evaluation

- The company shall submit the full registration dossier to the administration of human pharmaceuticals regulatory affairs within a maximum period of 30 months from the date of the registration request approval, Otherwise the Registration request approval shall be cancelled based on the report submitted from head of Central administration of pharmaceutical products and head of Central Administration of Operations to be approved by EDA Chairman, **any request for additional period has not been allowed.**

- The company shall submit the full registration dossier to the administration of human pharmaceuticals regulatory affairs after the following:
  a. Obtaining Registration request approval, Naming approval, PV approval, Pricing certificate and CADC Report (including Product conformity certificate and composition according to technical requirements attached).
  b. Production of three Pilot/ Production batches.
- The Administration of Human Pharmaceuticals regulatory affairs shall screen the full registration dossier within 7 working days.
- In Case of acceptance**,** administration of human pharmaceutical regulatory affairs shall **distribute** the registration dossier to the concerned administrations for technical evaluation within 60 working days.
- In the case that supplementary documents are required to be fulfilled after evaluation by any of the aforementioned administrations, the company shall be notified. The company shall submit the supplementary documents in a maximum period of 3 months.
- In the event that the total deadline for required completions is exceeded, the company is obligated to pay the service consideration for extending the deadline for completing completions for the General Administration of Human Pharmaceuticals Registration.
- Upon fulfilling all the requirements of all the concerned administrations, all the approvals shall be issued within a maximum of 10 working days.
- Module 1 shall be updated after getting the approvals.

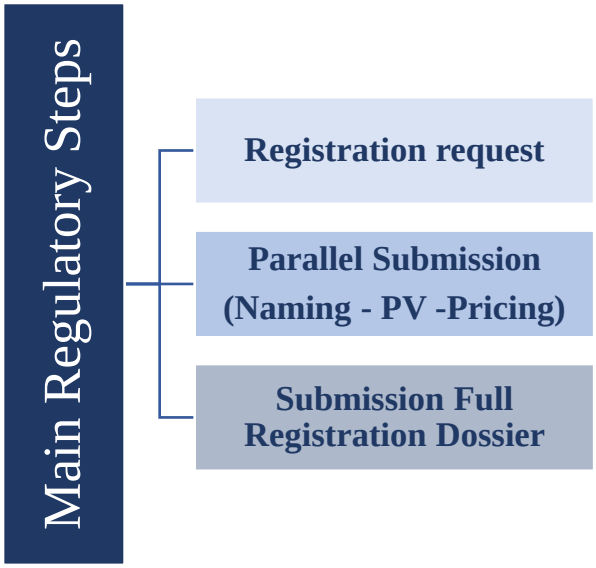
- The final review of the file shall be carried out by the Administration of human pharmaceutical Regulatory Affairs within 30 working days.
- In the case that Supplementary documents are required to be fulfilled after review, the company shall be notified by comments.
- The company shall submit the Supplementary documents in a maximum period of 30 working days.
- In the event that the total deadline for required completions is exceeded, the company is obligated to pay the service consideration for extending the deadline for completing completions for the General Administration of Human Pharmaceuticals Registration.
- The supplementary documents shall be reviewed by the Administration of human pharmaceutical Regulatory Affairs within 15 working days.
- In case the registration dossier is fulfilled, the Administration of human pharmaceutical Regulatory Affairs shall present it to the Technical Committee for Drug Control within 30 working days to adjudicate on the issuance of a registration license of the product.

Technical Committee for Drug Control Approval	Technical Committee for Drug Control Rejection
A final registration License valid for a period of 10 years shall be issued, provided that the company shall comply with the requirements mentioned in the license and the Central Administration of Operations shall follow up the company compliance.	The company shall be notified of the rejection by virtue of a letter containing the decision of the Technical Committee for Drug Control. The reasons of rejection shall be indicated. The company may submit an appeal to the General Administration of Human Pharmaceuticals Registration against the final decision issued by the Technical Committee for Drug Control within 60

	working days from the issuance date of the decision, by virtue of a reasoned request to be submitted to the Technical Committee for Drug Control, which request shall be supported by the documents and information that the company is desirous to rely on when its appeal is being considered. The matter shall be presented to the Technical Committee within 60 working days from the date when the appeal is submitted.

- **Required procedures to be implemented after the issuance of the registration license:**
  a. The production shall take place within 18 months from the issuance date of the final registration License.
  b. The accelerated and long-term stability studies for the first three production batches shall be completed within five years from the issuance date of the registration license, provided that the company shall submit the studies after completing them.

B) The Regulatory Procedures of Synthetic Peptides for Imported human pharmaceutical products



First: Procedures for obtaining the registration request approval:

- The company is obligated to submit a registration request in accordance with the regulatory mechanisms of the General Administration of Human Pharmaceuticals Registration published on the Egyptian Drug Authority website. This request shall be accepted in accordance with the date and time of its submission in complete and correct form, provided that the company shall receive acceptance of the initial acceptance of the registration request within 3 working days from the date of receiving the completed registration request.
- The company shall be notified of the **status** of the product within a maximum of 18 working days from the date of the initial Acceptance of the fulfilled registration request.

- In the case there are documents required to be fulfilled, the company shall be obligated to complete any required documents within a maximum of 3 months from the date of its notification.
- The registration request approval shall be issued within 10 working days from the date of receiving the fulfilled required documents. The Company shall be obligated to pay the consideration of product registration before heading for receiving the registration request approval, provided that the company shall receive the registration request approval within 30 working days from the date of its issuance, otherwise the registration request will be cancelled.

Notes:

- Only Imported products that **are marketed in one of reference countries** approved by the Technical Committee of Drug Control will be accepted.
- The number of registration requests available to be submitted per month shall be **counted** within the submission numbers of the specific registration requests, and in case the company is desirous to submit other registration requests in the same month, the company shall be obligated to **pay** the service consideration prescribed for additional requests other than the number permitted to be submitted per month.

Second: The company shall apply in parallel to the following departments:

1. Evaluation Unit for Trade Named and Mock-up of Human Pharmaceuticals

- The company shall be obligated to apply to the Evaluation unit for Trade Names and Mockup for Human Pharmaceuticals within 30 working days from the date of the registration request approval for getting approval for the product name, provided that name approval shall be issued within 15 working days from the date when the company applies to the Evaluation unit for Trade Names and Mockup for Human Pharmaceuticals.

2. Central Administration of Pharmaceutical Policies and Market Access /General Administration of Market Access and Business Continuity – Administration of Pricing Policies

- The required documents for pricing shall be submitted within 30 working days from the issuance date of the registration request approval, otherwise, the registration request will be cancelled based on a report submitted by the relevant central administration.
- The product shall be priced within a maximum period of 90 working days from the date of receiving the complete pricing file
- The pricing certificate must be issued within 6 months from the date of submission to the Pricing Administration.

3. Central Administration for Pharmaceutical Care / General Administration of Pharmaceutical Vigilance

The Pharmacovigilance Requirements shall be Submitted within 30 working days from the issuance date of the registration request approval according to the regulatory mechanism of the General Administration of Pharmaceutical Vigilance, otherwise, the registration request will be canceled based on a report submitted by the relevant central administration. The documents submitted by the company shall be evaluated within a maximum of 60 working days from the date of receiving the fulfilled pharmacovigilance documents (provided that the document describing the Pharmacovigilance system of the company shall be completed upon evaluation).

- **In case of the approval of General Administration of Pharmaceutical Vigilance**:

The company shall be notified of the approval and the product registration procedures shall be completed. In case the company is required to fulfill other documents, the company shall be given a period of a maximum of 30 working days

(this period may be renewed for one time, when necessary). The evaluation shall be finished by the General Administration of Pharmaceutical Vigilance within 30 working days from the date of receiving the required documents.

- **In case of non-approval or non-fulfillment of the documents**:

The registration request shall be presented to the Technical Committee for Drug Control by the General Administration of Pharmaceutical Vigilance to take the decision it deems appropriate and to state the reasons in the case of rejecting the registration request.

Third: Submission of Full Registration Dossier for evaluation

- The company shall submit the full registration dossier to the administration of human pharmaceuticals regulatory affairs within a maximum period of 6 months from the issue date of the Pricing certificate or Pharmacovigilance approval whichever is later, Otherwise the Registration request approval shall be cancelled based on the report submitted from head of Central administration of pharmaceutical products and head of Central Administration of Operations to be approved by EDA Chairman, **any request for additional period has not been allowed.**

- The company shall submit the full registration dossier to the administration of human pharmaceuticals regulatory affairs after Obtaining Registration request approval, Naming approval, PV approval, Pricing certificate.
- The Administration of Human Pharmaceuticals regulatory affairs shall screen the full registration dossier within 7 working days.
- In Case of acceptance**,** administration of human pharmaceutical regulatory affairs shall **distribute** the registration dossier to the concerned administrations for technical evaluation within 60 working days.
- In the case that supplementary documents are required to be fulfilled after evaluation by any of the aforementioned administrations, the company shall be notified. The company shall submit the supplementary documents in a maximum period of 3 months.
- In the event that the total deadline for required completions is exceeded, the company is obligated to pay the service consideration for extending the deadline for completing completions for the General Administration of Human Pharmaceuticals Registration.
- Upon fulfilling all the requirements of all the concerned administrations, all the approvals shall be issued within a maximum of 10 working days.
- Module 1 shall be updated after getting the approvals
- The final review of the file shall be carried out by the Administration of human pharmaceutical Regulatory Affairs within 30 working days.

- In the case that Supplementary documents are required to be fulfilled after review, the company shall be notified by comments.
- The company shall submit the Supplementary documents in a maximum period of 30 working days.
- In the event that the total deadline for required completions is exceeded, the company is obligated to pay the service consideration for extending the deadline for completing completions for the General Administration of Human Pharmaceuticals Registration.
- The supplementary documents shall be reviewed by the Administration of human pharmaceutical Regulatory Affairs within 15 working days.
- The product shall be presented to the Technical Committee for Drug Control within 30 working days from the date when the company fulfills the complete dossier, so that the Technical Committee shall take the appropriate decision whether to register the product or not.

Technical Committee for Drug Control Approval	Technical Committee for Drug Control Rejection
A final registration License valid for a period of 10 years shall be issued, provided that the company shall comply with the requirements mentioned in the license and the Central Administration of Operations shall follow up the company compliance.	The company shall be notified of the rejection by virtue of a letter containing the decision of the Technical Committee for Drug Control. The reasons of rejection shall be indicated. The company may submit an appeal to the General Administration of Human Pharmaceuticals Registration against the final decision issued by the Technical Committee for Drug Control within 60 working days from the issuance date of the decision, by virtue of a reasoned request to

	be submitted to the Technical Committee for Drug Control, which request shall be supported by the documents and information that the company is desirous to rely on when its appeal is being considered. The matter shall be presented to the Technical Committee within 60 working days from the date when the appeal is submitted.

Notes: For the imported products, **the analysis file** shall be submitted to the Central Administration for Drug Control, including the documents and attachments required for the analysis file of the first received shipment **after** the issuance of the registration license. The first received shipment shall not be released until the analysis result is issued from the Central Administration for Drug Control.

- **Required procedures to be implemented after the issuance of the registration license:**

Importation of the imported products that have a marketing authorization license in the Egyptian markets shall take place **within 18 months** from the issuance date of the marketing authorization license; otherwise, the marketing authorization license shall be cancelled based on a report issued by the Central Administration of Operations.

Technical File Requirements

The development and quality specifications

- As differences in impurities, particularly peptide-related impurities, may affect the safety or effectiveness of a peptide, high attention is directed toward the importance of understanding the generic synthetic peptides impurity profiles. Deletion, insertion, or modification of amino acid sequences or residues are the main roots of formation of new impurities that may increase the risk of immunogenicity. Therefore, adequate information to assess the impurity profile should elaborated in both drug substance and drug product. Purity control strategy should be established using orthogonal analytical methods to minimize the risk of undetected impurities coeluting with the main peak or with each other.
- Since certain properties, such as biological activity, secondary structure and oligomer/aggregation states may be affected by the formulation of the drug product, finished product considerations (e.g. choice of excipients, manufacturing & sterilization aspects) relevant to generic synthetic peptides products should be addressed and strictness to reference product is required.
- Hereafter, requirements for generic synthetic peptides concerning development and quality specifications are mentioned in table (1), The decision tree in Diagram (A) can be used as an aid.

Table (1): Development and quality specifications requirements for synthetic peptides pharmaceutical products that refer to a reference product of rDNA origin

	Drug Substance (DS)	Drug Product (DP)
Development		
Comparative physicochemical characterization and biological evaluation between generic synthetic peptide product and reference product	**R** The comparison should include the following parameters: - Primary sequence and physicochemical properties - Secondary structure - Oligomer/aggregation states	**NR[1]**

	- Biological activities	
Characterization of impurities (Peptide related impurities and non-peptide related impurities)	**R** (Comparison between the impurity profile of the synthetic peptide and reference product should be demonstrated. Any new related impurity from the reference product, its level should be no more than 0.5 percent of the drug substance) [2]	**R** (Complete stress study should be done on both generic and reference products to establish the sameness of their purity profile)
Quality specifications		
Identification (Two methods are required)	**R** Peptide mapping is required for longer sequences (e.g., >20 amino acids)	**R** Peptide mapping is required for longer sequences (e.g., >20 amino acids)
Assay	**R** Bioassay is required	**R** Bioassay is required to be a release test for the 1st three submission batches and a skip testing is accepted later on with correlation studies between the bioactivity and the routine assay in finished product and forced degraded samples.
Impurities[3] (Oligomers should be included[4])	**R**	**R**
General tests	**R**	**R**

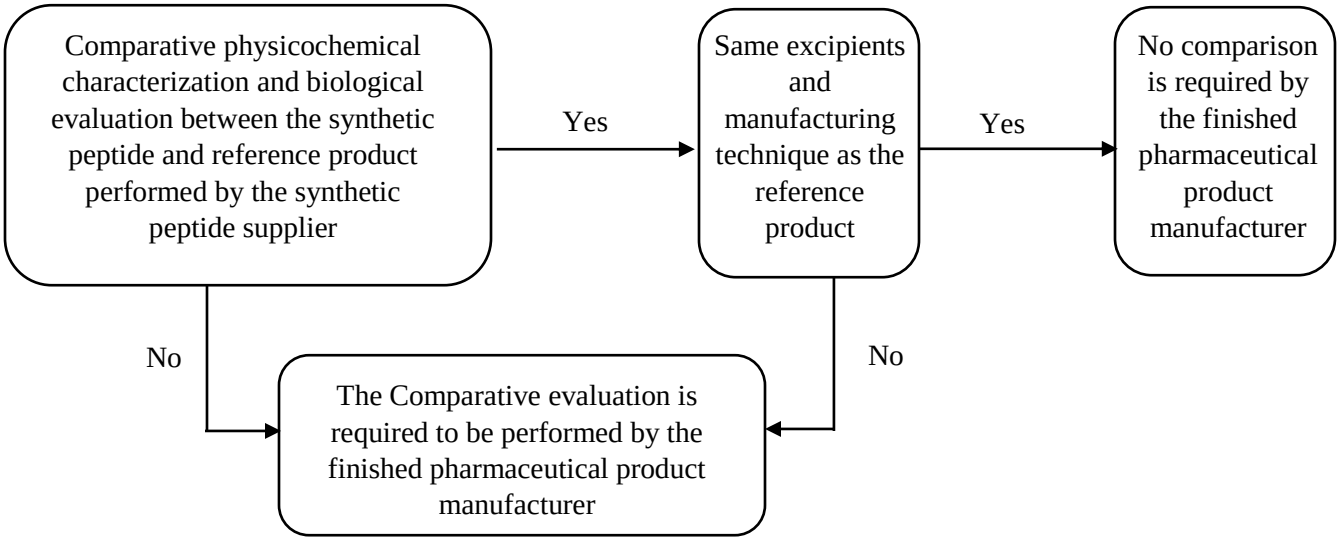
[1]In case of choosing different excipient or manufacturing technique other than the reference product, a comparison between generic synthetic peptide product and reference product will be required as per drug substance or if the comparison was not performed in the drug substance.

[2]Justification for why the presence of such new impurity would not be expected to affect the safety of the proposed generic synthetic peptide or its effectiveness as compared to that of the reference product, including with respect to the risk of immunogenicity.

[3]Sensitive and specific LC-HRMS method is recommended for characterizing peptide-related impurities.

[4]Size-exclusion LC for the determination of dimers and higher-molecular-mass impurities remains an important purity test as aggregated molecules may exhibit immunogenicity.

Diagram(A): Decision tree for comparative physicochemical characterization and biological evaluation requirement between the generic synthetic peptide product and reference product



- **General considerations for the container closure system:**
  In case of using a container closure system (cartridge) other than the reference product's one (pre-filled pen), a risk assessment should be done including a comparison between the two container closure systems with supportive data.

Stability Study

- The accelerated stability study shall be conducted for a period of six months on the three Pilot/Production batches and shall be accompanied with the composition that signed and stamped by the inspector of the Central Administration of Operations according to which the production was made.
- This study shall be conjoined with a long-term stability study for a period of at least one year that shall be conducted on the same pilot/production batches so that the product is entitled to be granted the **appropriate validity period according to the current ICH guidelines**, provided that the General Administration of Operations shall be notified of the place and time of performing the stability study before starting it.

Bioequivalence Study

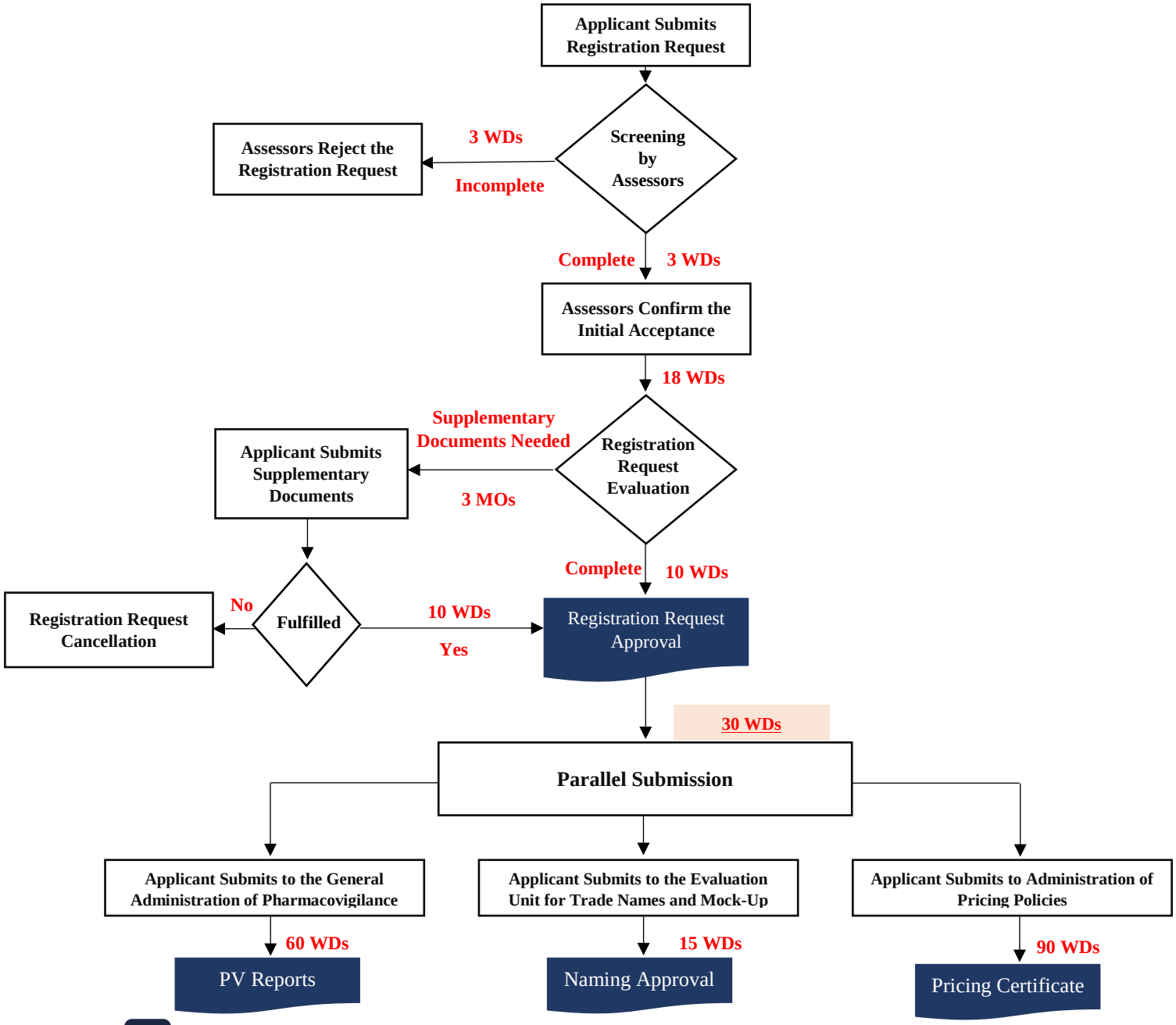
- The study of bioequivalence shall be conducted on the first Pilot/Production batch accompanied with the composition that signed and stamped by the inspector of the Central Administration of Operations according to which the production was made.
- The study shall be conducted according to the International guideline in one of the bioequivalence centers that are licensed by the Egyptian Drug Authority.

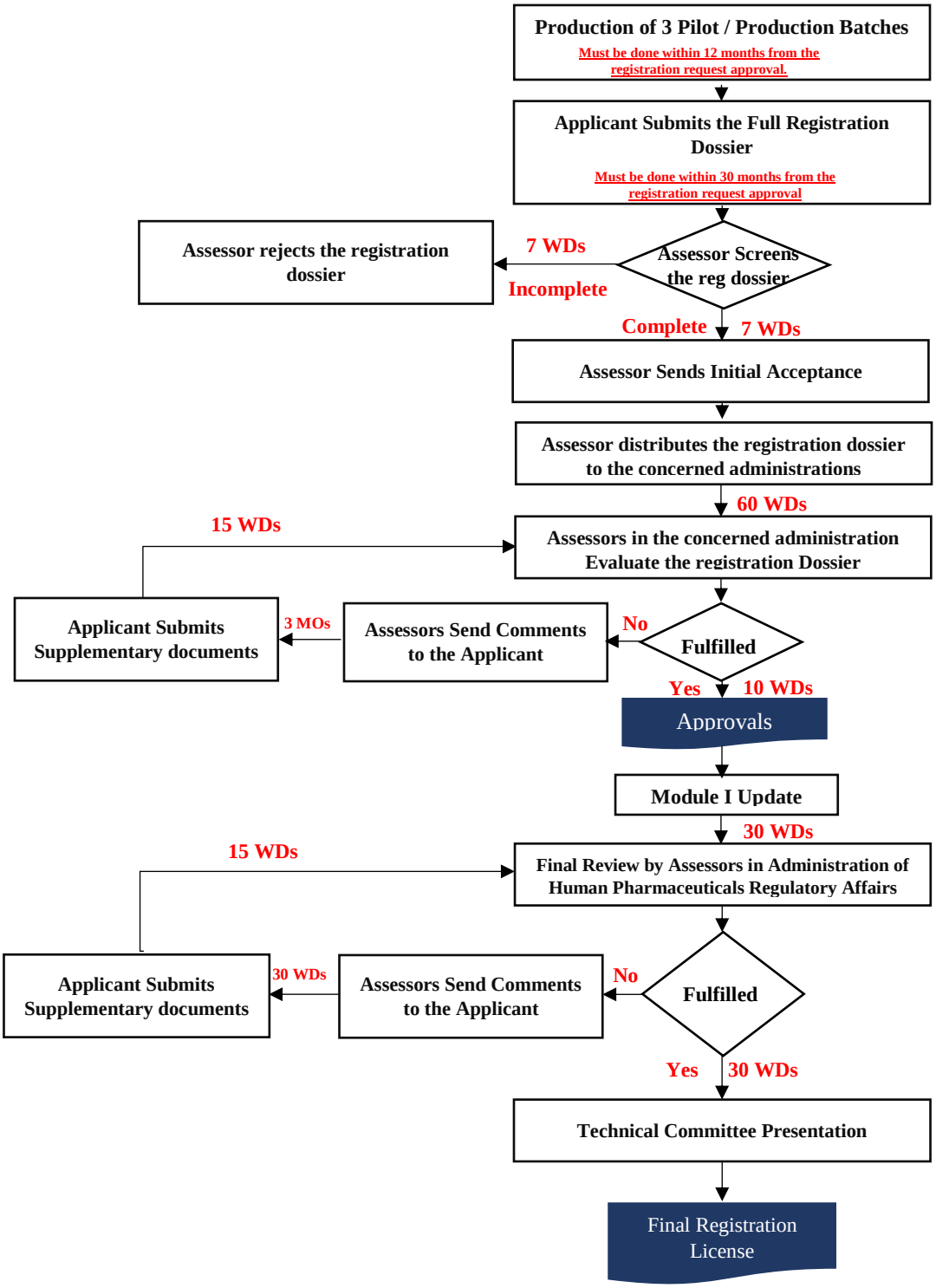
References

1. EDA chairman decree 450/2023
2. FDA Guidance for Industry ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin Guidance for Industry, May 2021.
3. USP <1503> QUALITY ATTRIBUTES OF SYNTHETIC PEPTIDE DRUG SUBSTANCES

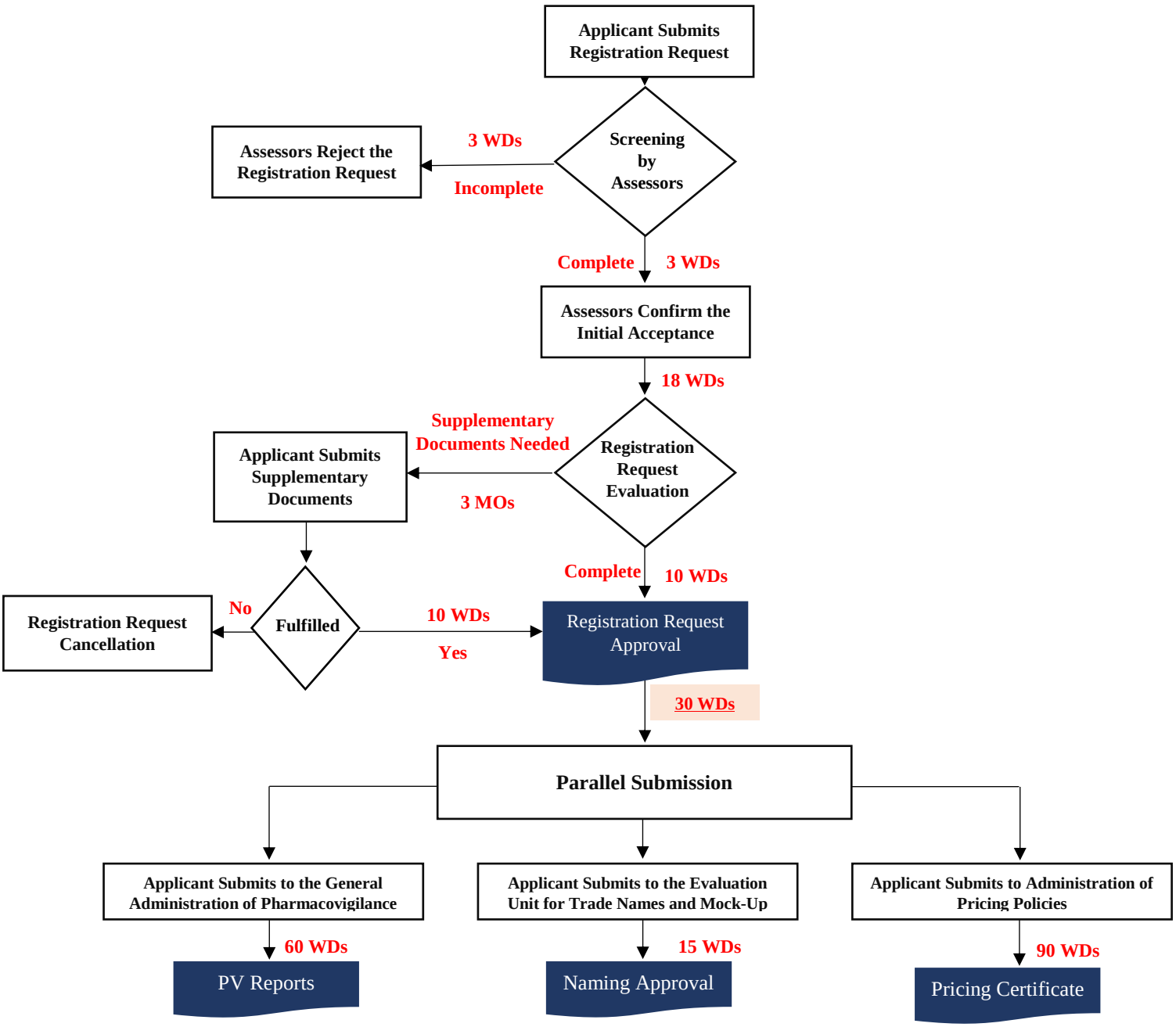
Annex I: Flowchart

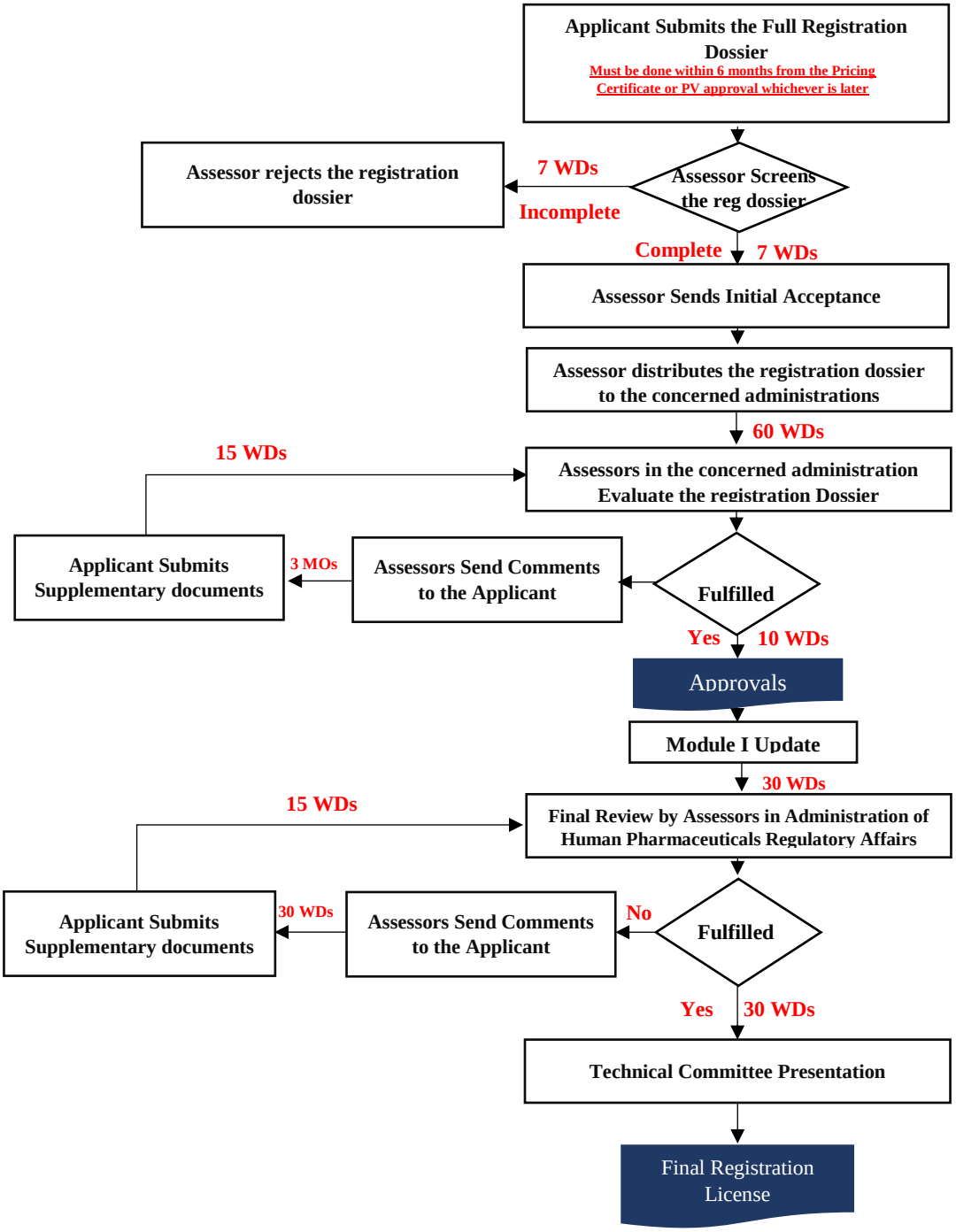
Flowchart for Locally Manufactured Synthetic Peptides




Production of 3 Pilot / Production Batches
Must be done within 12 months from the registration request approval.
Applicant Submits the Full Registration Dossier
Must be done within 30 months from the registration request approval
Assessor Screens the reg dossier
7 WDs
Incomplete
Assessor rejects the registration dossier
Complete
7 WDs
Assessor Sends Initial Acceptance
Assessor distributes the registration dossier to the concerned administrations
60 WDs
Assessors in the concerned administration Evaluate the registration Dossier
15 WDs
Fulfilled
No
Assessors Send Comments to the Applicant
3 MOs
Applicant Submits Supplementary documents
Yes
10 WDs
Approvals
Module I Update
30 WDs
Final Review by Assessors in Administration of Human Pharmaceuticals Regulatory Affairs
15 WDs
Fulfilled
No
Assessors Send Comments to the Applicant
30 WDs
Applicant Submits Supplementary documents
Yes
30 WDs
Technical Committee Presentation
Final Registration License

Flowchart for Imported Synthetic Peptides




Applicant Submits the Full Registration Dossier
Must be done within 6 months from the Pricing Certificate or PV approval whichever is later
Assessor Screens the reg dossier
7 WDs
Incomplete
Assessor rejects the registration dossier
Complete
7 WDs
Assessor Sends Initial Acceptance
Assessor distributes the registration dossier to the concerned administrations
60 WDs
Assessors in the concerned administration Evaluate the registration Dossier
15 WDs
Fulfilled
Assessors Send Comments to the Applicant
3 MOs
Applicant Submits Supplementary documents
Yes
10 WDs
Approvals
Module I Update
30 WDs
Final Review by Assessors in Administration of Human Pharmaceuticals Regulatory Affairs
15 WDs
Fulfilled
Assessors Send Comments to the Applicant
30 WDs
Applicant Submits Supplementary documents
No
Yes
30 WDs
Technical Committee Presentation
Final Registration License

Annex II: Frequently Asked Questions (FAQs)

1. **What are the peptide drug products covered under the regulatory guide?**

The regulatory guide provides recommendations for evaluation of synthetic peptide that references any of the following peptide drug products of r DNA origin:

- Glucagon & glucagon like- peptides as semaglutide
- Liraglutide
- Nesiritide
- Teriparatide
- Teduglutide

2. **Can the regulatory guide be applied for other kinds of peptide drug products?**

   The recommendations for evaluation of synthetic peptides that reference peptide drug products of rDNA origin can be applied for evaluation of other types of synthetic peptides e.g. Tirzepatide

3. **Are there different grades of APIs of synthetic peptides that reference peptide drug products of rDNA origin?**

   The APIs of synthetic peptides have different grades according to their route of administration as oral or injectable grades with different specifications in bacterial endotoxin and sterility tests.

4. **Is comparative physiochemical characterization and biological evaluation between generic synthetic peptide product and reference product required?**

Comparative physiochemical characterization and biological evaluation between generic synthetic peptide products and reference product is required including:

- Primary sequence
- Secondary structure
- Oligomer aggregation states
- Biological activities

5. **What are the different types of impurities should be controlled in the specifications of the peptide drug product?**

   There are different types of impurities should be controlled in the specifications of peptide drug products including but not limited to the following:

   - Peptide-related impurities
   - Oligomers

6. **Is bioassay required to be added in the specifications of the peptide drug product?**

   Bioassay is required as mandatory test in the specifications of the 1st three submission batches and can be then added as a skip testing with correlation studies between bioactivity and the routine assay in finished product and forced degraded samples.

7. **Is peptide mapping required as identification test for the peptide drug product?**

Peptide mapping is required as a mandatory identification test for longer sequence peptide drug products (e.g. > 20 amino acids)

8. **Should particle size of API be controlled in the peptide drug product?**

   Particle size should be controlled for API in oral peptide drug products as it may have an impact on drug products` performance.

9. **Can we use a different pre-filled pen for the generic peptide drug product than the pre-filled pen of the reference product?**

   The use of different pre-filled pen for the generic peptide drug products than the pre-filled pen of the reference product requires full detailed comparative study between the two pens including but not limited to the following tests:
   - Accuracy of delivered dose.
   - Mechanical functionality.

10. **What are the required stability studies for peptide drug products at the time of submission?**

Six months accelerated stability study and 12 months long term stability study for 3 pilot/production batches of peptide drug products should be submitted.

Submitting less than 12 months long term stability study for 3 pilot/production batches is not accepted.

Document History

Version number	Issue Date	Summary of Change
1	03-12-2023	New Issue
2	10-12-2024	- Addition of Annex II (Frequently asked questions) - Addition of Document history table to clarify the amendments in versions of the guideline
3	6-3-2025	- Change in Scope - Addition of The Regulatory Procedures of Synthetic Peptides for Imported human pharmaceutical products. - Addition of Annex Flowchart for Imported Synthetic Peptides