Central Administration for Pharmaceutical Products
General Administration of Veterinary Pharmaceuticals

Guideline

Guideline on Veterinary Pharmaceuticals Variations

Year 2024

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1. Background:

This guidance document is intended to provide supportive information on how to present an application to implement a variation to a veterinary medicinal product.

Changes to the details of the product in order to accommodate technical and scientific progress, or to improve or introduce additional safeguards for the registered veterinary product are referred to as variations.

Requirements for the different types of variations are set out in this guidance in order to facilitate the submission of appropriate documentation by applicants and their assessment by EDA and to ensure that variations to the veterinary medicinal product do not result in health concerns.

*This guidance supersedes the guidance published in 2019.

1.1 Objective:

These guidelines are intended to:

- Assist applicants with the classification of changes made to the registered veterinary medicines
- Provide guidance on the technical and other general data requirements to support changes made to the registered veterinary medicines

1.2 Scope:

This guidance document is applicable to veterinary pharmaceuticals variations.

2. Definitions:

Variations: Administrative &/or post-authorization changes that take place on the post marketed finished pharmaceutical product or active pharmaceutical ingredients.

Submission Guidance: List of Required documents used by companies to fulfill the submitted variation requests.

Final approval: Letter stating that EDA approved the change submitted by the applicant company after fulfilling the required studies.

Finished Pharmaceutical Product (FPP): The dosage form in the final immediate packaging intended for marketing.

Active substance: Any substance or mixture of substances having pharmacological activity intended to be used in manufacture of FPP.

Excipient: Any substance or compound other than active substance and packaging materials that intended to be used in manufacture of FPP.

Container closure system: The sum of packaging components that together contain and protect pharmaceutical product, including primary and secondary packaging components.

Production Batch: A batch of FPP manufactured at production scale by using production equipment in a production facility.

3. Procedures

3.1 Overview on handling variation requests:

These guidelines include specific examples of changes. However, it should be noted that a change not covered by these guidelines, should be evaluated through a risk-based assessment.
It remains the responsibility of the applicant to submit relevant documentation to justify that the change will not have a negative impact on the quality, safety and efficacy of the product. In addition, the applicant is responsible to notify the Variation Administration in EDA in case of any unfavorable out of specification that has negative impact on the quality of the finished pharmaceutical products.
The applicant will apply the variation request according to the submission guidance.
For all variations when accelerated stability study for 6 months is required, the applicant company should place the first production-scale batch of the FPP produced with the new variation into the long-term stability program to be conducted and the applicant company is responsible to notify the Variation Administration in EDA in case of any unfavorable out of specification that has negative impact on the quality of the finished pharmaceutical products.

3.2 Variation Evaluation Routes

3.2.1 Full Evaluation Route:

Full evaluation will apply to variations subject to EDA full review and assessment prior to change. The procedure starts from the date of submission of a valid payment receipt and variation request. Then, the application will undergo initial review and technical evaluation by the concerned unit of variation. By the end of the technical evaluation period, the variation administration will determine its decision on the variation request and inform the applicant about the acceptance or rejection of the variation. For Further consultation, the variation request may be subjected to variation evaluation committee (VEC) or to technical committee for drug control (TCDC) or both.

3.2.2 Reliance Evaluation Route:

For imported products, the variation administration will implement regulatory reliance for assessment of variations that were already approved by other reference countries (SRAs–Annex III).

Reliance on other SRAs involves leveraging the assessments and evaluations conducted by trusted regulatory agencies instead of duplicating the entire evaluation process. However, EDA remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others.

The application should be identical to that approved by the SRA in terms of dosage form, strength and formulation (as applicable) and the applicant should therefore confirm and attest that the information (variation dossier) submitted to the EDA is the same as that submitted to reference SRA along with a copy of the reference SRA decision or other document confirming the final decision of the reference SRA.

When submitting proof of the SRA final decision, EDA acknowledges the different evaluation criteria, variation categorization and approval process between each individual SRA as well as the difference between the SRA and the EDA procedures.

4. General Consideration

4.1 Post Market Changes for Specifications & Composition Variation

4.1.1 Administrative Changes Concerning Specifications & Composition Variation

	Requirements	
	CADC	**Stability**
4.1.1.1 Change in name of active substance or of an excipient	**None**	**None**
Condition to be fulfilled The substance shall remain the same		

4.1.2 Quality Changes Concerning Specifications & Composition Variation

4.1.2.1 Description and composition

4.1.2.1.1 Change in the composition (excipients) of the finished pharmaceutical product		**Requirements**	
		CADC	**Stability**
a) Changes in components of the flavoring or coloring system			
1	Addition, deletion or replacement	**A***	**6M****
2	Increase or reduction not more than 10%	**A***	**None**
b) Other (excipients)			
1	Replacement of a single excipient with a comparable excipient with the same functional characteristics and same quantity at a similar level.	**A***	**6M****
2	Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the medicinal product	**A***	**6M****
3	Clarification /Change of excipients functions for non-functional excipients	**None**	**None**
4.1.2.1.2 Changing / Clarifying Active/In active Ingredient Specification			
1	Change from one pharmacopeia to another pharmacopeial specification.	**N*****	**None**

2	Change from pharmacopeial specification to in-house specification. (If change is within pharmacopeial limits)	**A***	**6 M****
3	Change from in-house specification to pharmacopeial specification.	**N*****	**None**
4	Clarifying specification for active ingredient (if API specs: in house)	**A***	**6 M****
5	Clarifying specification for active ingredient (if API specs: pharmacopeial specs)	**N*****	**None**
6	Addition of Another Pharmacopeial Specification for active /in actives.	**None**	**None**
7	Clarification /Change of excipients Specifications.	**None**	**None**
4.1.2.1.3 Changing / Clarifying salt equivalence and crystalline state			
1	Change in salt equivalence and crystalline state (e.g., hydrate, solvate, Polymorph…)	**A***	**6M****
2	Clarification of salt equivalence and crystalline state (e.g., hydrate, solvate, Polymorph…)	**None**	**None**
4.1.2.1.4 Change in particle size for water Insoluble or sparingly soluble API (particle size must be stated in suppliers COA by D90 or mesh size)		**A***	**6M****
4.1.2.1.5 Addition of an overage to the drug product manufacturing batch formula to compensate manufacturing losses (for active ingredients or preservatives only).		**A*** **based on overage percentage**	**None**

Requirements guidance:

* Batch Analysis for first production batch at CADC labs.

** Result of stability testing generated on first production batch with a minimum of 6 months accelerated testing.

***Notification.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2-Relevant Documents According to Composition & Specification variation type:

Change in name of active substance or of an excipient
Required documents
1-Old composition "signed and stamped".
2-New composition "signed and stamped".
3-Comparison table between old and new composition
4-Pharmacopeial monograph for active ingredient or reference for the name of inactive ingredient.

Change in the composition (excipients) of the finished pharmaceutical product/ Elimination, Reduction or Addition of an overage
Required documents
1-Old composition "signed and stamped".
2-New composition "signed and stamped".
3-Comparison table between old and new composition “signed and stamped".
4-Scientific justification & Reference and write in composition the cause of Addition (e.g., for Manufacturing loss) (In case of Addition of an overage).

Change / Clarification of Active/ Inactive Ingredient Specification
Required documents
1-Old composition "signed and stamped".
2-New composition "signed and stamped".
3-Comparison table between old and new composition “signed and stamped".
4-Pharmacopeia Monograph (Last Edition)
5-Comparison between Old & New Finished Pharmaceutical Product Specification signed and stamped.
6-Import plans or approvals, Customs releases, invoices and supplier certificates, have the same batch numbers that were imported for three consecutive years. (In case of clarifying Specifications of Active Ingredient)
Clarification/Change of salt equivalence and/or crystalline state (E.g., hydrate, solvate, polymorph)
Required documents
1-Old composition "signed and stamped".
2-New composition "signed and stamped".
3-Comparison table between old and new composition. “Signed and stamped".
4-Scientific Reference for Molecular weight of base and salt. (e.g., Pharmacopeia).
5-Calculations of salt equivalence on company paper signed and stamped.
6-In case of clarification: a report from Inspection Department stating the form of used materials including batch record and any previous studies on the same batch.
7-In case of clarification: Import plans or approvals, Customs releases, invoices and supplier certificates, have the same batch numbers that were imported for three years.
Clarification /Change in particle size for water Insoluble or sparingly soluble API (Particle size must be stated in suppliers COA by D90 or mesh size)
Required documents
1-Old composition "signed and stamped".
2-New composition "signed and stamped" (State Range of D90 in New Composition).
3-Comparison table between old and new composition “signed and stamped".
4-C.O.A of all suppliers for active ingredient stated D 90 or mesh size
5-A report from Inspection Department stating the Range of D90 of used materials (In case of Clarifying Particle Size)

6-Import plans or approvals, Customs releases, invoices and supplier certificates, have the same batch numbers that were imported for three years (In case of Clarifying Particle Size).			
4.1.2.2 Control of finished pharmaceutical product			
4.1.2.2.1Change in the specification parameters and/or limits of the finished pharmaceutical product		**Requirements**	
		CADC	**Stability**
a	Tightening of specification limits	**None**	**None**
Condition to be fulfilled 1. The test procedure shall remain the same, or changes in the test procedure shall be minor 2. The change should be within the range of currently approved limits.			
b	Deletion of a non-significant specification parameter (e.g., deletion of an obsolete parameter such as odor and taste or identification test for a coloring or flavoring material)	**None**	**None**
Condition to be fulfilled 1. The change shall not relate to an unexpected event during manufacture. 2.The change shall not concern a critical parameter or have the potential to affect the identity, strength, quality, purity, potency or physical characteristics of the finished product			
c	Addition of a new specification parameter to the specification with its corresponding test method	**A***	**None**
d	Widening of specification limits “the change is not the result of unexpected events arising during manufacture”	**A***	**6M****
e	Change the Pharmacopeial product from Pharmacopeial product to Non pharmacopeial one	**A***	**6M****

4.1.2.2.2 Change in the shelf life or storage conditions of the finished pharmaceutical product		Requirements	
		CADC	Stability
a	Extension of the shelf life of the finished pharmaceutical product As packaged for sale (supported by real time data) After first opening (supported by real time data) After dilution or reconstitution (supported by real time data)	None	Approval from Stability Administration for proposed Change.
b	Change in storage conditions of the finished pharmaceutical product or the diluted/reconstituted product	None	Approval from Stability Administration for proposed Change
Condition to be fulfilled -Approval from Stability Administration for proposed change.			
c	Reduction of the shelf life of the finished product as packaged for sale, after first opening or after dilution or reconstitution	None	None
Condition to be fulfilled The change shall not be the result of unexpected events arising during manufacture or because of stability concerns**.**			

Requirements guidance:

* Batch Analysis for first production batch at CADC labs.

** Result of stability testing generated on first production batch with a minimum of 6 months accelerated testing.

***Notification

Submission guidance:

1 -Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2-Relevant Documents According to Composition & Specification Variation type:

(Control of finished pharmaceutical product)

Change in the specification parameters and/or limits of the finished pharmaceutical product
Required documents
1- Old finished pharmaceutical product specifications "signed and stamped"
2- New finished pharmaceutical product specifications "signed and stamped"
3- Comparison table between old and new finished pharmaceutical product specifications
4- Scientific justification & Reference for the requested change
5-Pharmacopeia Monograph
6- Scientific Reference for Finished Pharmaceutical Product PH (In Case of Change PH Range)
Change in the shelf life or storage conditions of the Finished Pharmaceutical product **Reduction of the shelf life**
Required documents
1- Scientific Justification for this Reduction
2-Any Stability studies or documents for new shelf life clarifying the need of reduction of shelf life must be submitted
3- **In case of imported or under license files:** declaration letter from LH/MAH in COO signed and stamped, stating reasons of reduction.
Change in the shelf life or storage conditions of the Finished Pharmaceutical product **Extension of the shelf life**
Required documents
Stability study approval
Change in the storage conditions of the Finished Pharmaceutical product or the diluted/reconstituted product
Required documents
Stability study approval

4.1.2.3 Change in Physical Character of Finished Product:		Requirements	
		CADC	Stability
a	Change in range of color without any qualitative or quantitative change in excipients or active ingredients (To be as the stated color in CADC COA)	N	None
b	Change in range of color without any qualitative or quantitative change in excipients or active ingredients (The Color Range differs from what is stated in CADC COA)	A*	None or stability **6M if needed
Condition to be fulfilled -The change shall not affect the delivery, use or safety of the finished product. -The finished product release and shelf-life specifications shall not have been changed except for appearance.			
c	Change in scoring /break lines not intended to divide the FPP into equal doses	None	None
d	Change in scoring /break lines intended to divide into equal doses	A*	None

Requirements guidance:

* Batch Analysis for first production batch at CADC labs.

** Result of stability testing generated on first production batch with a minimum of 6 months accelerated testing.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2-Relevant Documents According to Composition & Specification Variation type:

(Change in Physical Character of Finished Product)

Change in color of finished product
Required documents
1- Sample (IF needed)
2- Old & new certificate of analysis
3- Pharmacopeia monograph & certificate of analysis of supplier of active ingredient (In case of change in range of color without any qualitative or quantitative change in composition)
4- Scientific Justification for color change with scientific reference
5- Manufacturing process flow chart (In case of the change in physical character is due to change in manufacturing process).

Change in scoring configuration
Required documents
1-Old composition "signed and stamped". (If needed)
2-New composition "signed and stamped". (If needed)
3- Safety data sheet for Ink including composition of ink (In case of change or addition of imprints)
4- Reference for scoring (In case of change of scoring/break lines on tablets).

4.1.2.4 Change in Container closure system			
4.1.2 4.1Change in primary packaging of the finished pharmaceutical product		**Requirements**	
		CADC	**Stability**
a)	Qualitative and quantitative packaging (composition within the same packaging type)		
1. Sterile medicinal products / Semi-solid and non-sterile liquid pharmaceutical forms		**A***	**6M****
2. Solid pharmaceutical forms		**None**	**6M****
Condition to be fulfilled The change only concerns the same packaging container type			
b)	Change to a new type of packaging container such as glass to plastic or addition of a new container	**A***	**6M****
4.1.2.4.2 Change in any part of the primary packaging material not in contact with the finished product formulation (such as change of color due to different plastic used for flip-off caps, color code rings on ampoules or change of needle shield		**None**	**None**
Condition to be fulfilled The change shall not concern a part of the packaging material that affects the delivery, use, safety or stability of the finished product			
4.1.2.4.3 Change in shape or dimensions of the container or closure (immediate packaging)			
1. Non sterile finished product		**None**	**None**
Condition to be fulfilled -The change shall not concern a part of the packaging material, which affects the delivery, use, safety or stability of the finished product. -The change shall not concern the qualitative or quantitative composition of the container.			
2. Sterile finished product		**A***	**6M****
4.1.2.4.4 Change in pack size of the finished product			
a)	Change in pack size (number of units e.g., tablets, ampoules, etc. in a pack)	**None**	**None**

Condition to be fulfilled The primary packaging material shall remain the same			
b)	Change in the fill weight/fill volume of non-sterile multi-dose medicinal products	**None**	**6M****
C)	Change in the fill weight/fill volume of sterile multi dose medicinal products	**A***	**6M****

Requirements guidance:

* Batch Analysis for first production batch at CADC labs.

** Result of stability testing generated on first production batch with a minimum of 6 months accelerated testing.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III
(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2-Relevant Documents According to Composition & Specification Variation type:

(Change in Container closure system)

Change in Container closure system
Required documents
1-Cover letter clarifying full detailed description for type of old / new pack its capacity and liner
2-Sample "If needed
3-Factory license with suitable production line "in case of change to a new type of container or addition of a new container

4.2 Post Market Changes for API for veterinary pharmaceuticals		
4.2.1 Administrative Changes concerning API		
	Requirements	
	CADC	**Stability**
4.2.1.1 Change in Name and/ or Address of Manufacturer of the active substance	**None**	**None**
Condition to be fulfilled -The manufacturing site and all manufacturing operations must remain the same.		
4.2.1.2 Deletion of manufacturing sites for an active substance	**None**	**None**
Condition to be fulfilled -There shall at least remain one site/manufacturer, as previously authorized performing the same function as the one(s) concerned by the deletion.		

4.2.2 Quality Changes concerning API		
	Requirements	
	CADC	**Stability**
4.2.2.1 Introduction of a new manufacture	**A***	**6 M****

Requirements guidance:

*Analysis of the first production batch of Finished Pharmaceutical product manufactured from the APImanufacturer at CADC labs.

**Results of stability testing generated with a minimum of 6 months Accelerated testing, and to be released to the market by Central Administration of Operation (Inspection Department) after evaluating the results of a minimum of 3 months of the first production batch of Finished Pharmaceutical product manufactured with the new API manufacturer.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2- Relevant Documents According to variation type of API for veterinary pharmaceuticals:

Change in the name and/or address of a manufacturer of the active substance	
1	Recent API Manufacturer certificate with the new name as the same address mentioned in old name certificate, submit one of the following: ▪ GMP. ▪ ISO 9001 – 2015 (for Minerals, Vitamins and Extracts only). ▪ CPP. ▪ Written confirmation letter. **In case of new name certificate is not including API:** Complete & recent API manufacturer license (or CPP) with the same new name certificate address & mentioning the API(s) name.
2	API Manufacturer certificate with the old name as the same address mentioned in new name certificate,submit one of the following: ▪ GMP. ▪ ISO 9001 – 2015 (for Minerals, Vitamins and Extracts only). ▪ CPP. ▪ Written confirmation letter.
3	**In case of local API(s) manufacturer(s), Submit one of the following:** **For current & required to be added manufacturer(s), submit one of the following:** ▪ API Manufacturer License issued from Egyptian Drug Authority mentioning the API production line. ▪ Data Certificate with API Manufacturer name issued from Egyptian Drug Authority mentioning theAPI production line.
4	**In case of the new name GMP is not issued yet:** **Declaration letter** from the authority which is responsible for the manufacturer inspection declares the name change without changing the manufacturing site (location).
5	**API variation Notification Form (template 2)**

Deletion of manufacturing sites for an active substance	
1	For **Current** API manufacturer(s)**, Submit one of the following:** ▪ GMP. ▪ ISO 9001 – 2015 (for Minerals, Vitamins and Extracts only). ▪ CPP. ▪ Written confirmation letter.
2	For **Current local** API manufacturer(s)**, Submit one of the following:** ▪ API Manufacturer License issued from Egyptian Drug Authority mentioning the API production line. ▪ Data Certificate with API Manufacturer name issued from Egyptian Drug Authority mentioning theAPI production line.
3	**API variation Notification Form (template 2)**

Introduction of a new manufacture	
1	**For API manufacturer(s) to be added, Submit one of the following:** ▪ GMP. ▪ ISO 9001 – 2015 (for Minerals, Vitamins and Extracts only). ▪ CPP. ▪ Written confirmation letter. **N.B.:** the submitted certificate is required to be complete, recent, mentioning the API(s) manufacturer name & its address & the API(s) name(s). **N.B.: if the submitted certificate does not mention the API(s) name:** Submit a complete, recent API(s) manufacturer license (or CPP) with the same address of GMP certificate & mentioning the API(s) name.
2	**In case of local API(s) manufacturer(s), Submit one of the following:** ▪ API Manufacturer License issued from Egyptian Drug Authority mentioning the API production line. ▪ Data Certificate with API Manufacturer name issued from Egyptian Drug Authority mentioning theAPI production line.
3	**API(s) manufacturer(s) CoA(s)**, it should fulfill the following: ▪ With the same specification of the API in the product registration license composition. ▪ Matching with API monograph in all tests and specification limits ranges. ▪ Mentioning the expiry date or re-test date.
4	**In case of the submitted CoA on manufacturer letter head Different from the API manufacturer:** Relationship Declaration Letter between the two manufacturers is required.
5	Updated Pharmacopeia Monograph for API(s).
6	**API variation Notification Form (template 2)**

4.3 Post Market Changes Concerning Ownership /Manufacturer of Finished Product		
4.3.1 Administrative Changes concerning Ownership /Manufacturer of finished product		
	Requirements	
	CADC	**Stability**
4.3.1.1 Change in Name and/or Address of FPP License Holder or Marketing Authorization Holder	**None**	**None**
Condition to be fulfilled -Product License Holder and/or Marketing Authorization Holder shall remain the same legal entity.		
4.3.1.2 Change in Name and/or Address of Manufacturing sites (including bulk manufacturer, packager & batch releaser)	**None**	**None**
Conditions to be fulfilled -The physical location of the manufacturing site and all manufacturing operations must remain the same		
4.3.1.3 Change in Applicant (Imported FPP)	**None**	**None**
Conditions to be fulfilled -The applicant shall be authorized for registration.		
4.3.1.4 Modification of registration license	**None**	**None**
Conditions to be fulfilled -Approval of EDA relevant department (s) on related modification.		
4.3.1.5 FPP License Holder or Marketing Authorization Holder transfer	**None**	**None**
Conditions to be fulfilled -The new FPP LH/MAH is a different legal entity. -If there is another product registered or under registration with the same name in the old company, either one of the products' names should be changed. - If the product is a line extension to a product registered or under registration owned by the new company, the names should be unified.		

4.3.1.6 Addition/Change of FPP MAH in Egypt (Imported, UL & Bulk FPP)	**None**	**None**
Conditions to be fulfilled: - FPP MAH in Egypt must comply with all FPP specifications, composition and all manufacturing operations as mentioned in the FPP CPP from NRA in the country of origin.		
4.3.1.7 Change/addition Supplier of solvent for a FPP (Local & UL FPP)	**None**	**None**
Conditions to be fulfilled -Solvent from new supplier must be registered. -Shelf life of solvent from new supplier must comply with shelf life of the FPP. -Pack of solvent from new supplier must comply with previously approved pack.		

Submission guidance

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2- Relevant Documents According to Ownership & Manufacturer variation type:

Change in Name / Address of FPP LH/MAH (Local FPP)	
1	**Declaration Letter** With list of all products affected by this name change. *Signed & stamped.
2	**Declaration Letter** The proposed company trade name in English *Signed & stamped.

Change in Name / Address of FPP LH/MAH (Imported, UL & Bulk FPP)	
1	**Declaration Letter** From LH/MAH Stating that it's the same legal entity with no change in LH/MAH, product specifications, quality, composition,manufacturing site & process. Authenticated from Chamber of commerce & Egyptian consulate/embassy
2	**Official document from a relevant official body** In case of changing address Justifying the change in address

Change in Name / Address of Manufacturing sites (Local FPP)	
1	**Declaration Letter** With list of all products affected by this name change. *Signed & stamped.
2	**Declaration Letter** The proposed company trade name in English *Signed & stamped.

Change in Name / Address of Manufacturing sites (Imported, UL & Bulk FPP)	
1	**No Change Declaration Letter** From LH Stating that there's no change in the physical location of the manufacturing site, manufacturing process, quality &composition of the product. Authenticated from Chamber of commerce & Egyptian consulate/embassy
2	**Certificate of Good Manufacturing Practice (GMP)** For the Site with the new name/address Valid Authenticated from Chamber of commerce & Egyptian consulate/embassy
3	**Certificate of Good Manufacturing Practice (GMP)** For the Site with the old name/address Authenticated from chamber of commerce & Egyptian consulate/embassy
4	**Official document from a relevant official body** In case of changing address Justifying the change in address

Change in Applicant for Registration (Imported, UL & Bulk FPP)	
1	**In Case of Imported finished Pharmaceutical Product if the applicant is either Scientific Office or Company the following documents to be submitted:** ***Scientific Office:** **a) "Authorization letter for the scientific office to register finished Imported Pharmaceutical Products"** Issued by inquiry requests unit for veterinary pharmaceuticals. **b) Declaration Letter** clarifying the company's profile code signed & stamped ***Company:** **Declarations Letter** clarifying the company's profile code describing its activity as "company authorized forregistration" And if not available The company must apply to Systems & Information Unit for creating a Company Profile to be able to submit variation requests

2	**Termination letter** From LH The Product trade Name & Reg. no. is mentioned Name & address of old Applicant mentioned Authenticated from chamber of commerce from country of origin & the Egyptian consulate/embassy + Original Arabic translation from a certified translation center **Or Waiver** From Old Applicant The product trade name & reg. no. is mentioned Authenticated from bank
3	**Authorization Letter** From LH The Product trade name & Reg. no. is mentioned Name & address of new applicant mentioned Clarifying its responsibilities for registration, all regulatory activities & signing contracts. Authenticated from chamber of commerce from country of origin & the Egyptian consulate/embassy + Original Arabic translation from a certified translation center. OR **Agency Agreement between** LH **and new Applicant** The Product trade name & reg. no. is mentioned Name & address of new applicant mentioned (as written in its commercial register) Clarifying its responsibilities for registration & all regulatory activities. Authenticated from chamber of commerce from country of origin & the Egyptian consulate/embassy + Original Arabic translation from a certified translation center
4	**Last Updated Commercial Register** For old applicant **OR Scientific office License** In case of scientific office
5	**Manufacturing contract** For UL FPP, between new applicant & manufacturer. Authenticated from Chamber of Commerce, Egyptian Consulate/Embassy, EDA Legal Affairs and Bank
6	**Attached Annex** Mentioning the product name & reg. no.

Modification of Registration License	
1	**EDA Approval** Of the required change to be updated in the registration license issued from relevant EDA department

FPP LH/ MAH Transfer (Local FPP)	
1	**Cover letter on new LH head letter clarifying the proposed change** Authenticated from Bank
2	**Ownership Waiver** From old LH to new LH Authenticated from Real Estate Registry at Ministry of Justice Authenticated from EDA Legal Affairs Product trade name, strength, dosage form & reg.no. is mentioned
3	**Manufacturing contract** Between LH & manufacturing site, valid& Authenticated from Bank & EDA Legal Affairs
4	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
5	**Composition declaration** On new LH head letter Identical to the one attached with the registration license or to the latest finally approved compositionSigned & stamped
6	**Declaration Letter: (Template 3)** From old LH, declaring all registered & under registration veterinary products containing the same active ingredient, Signed & stamped.
7	**Declaration Letter: (Template 3)** From new LH, declaring all registered & under registration veterinary products containing the same active ingredient, Signed & stamped
8	**Declaration Letter: (Template 4)** From new LH Stating all owned registered & under-registrations veterinary products (In case of Toll -under construction companies) Signed & stamped.
9	**Declaration Letter** No change in composition, specifications, manufacturing process, or container/closure system of the FPP, signed & stamped.

FPP LH/ MAH Transfer (Imported, UL & Bulk FPP)	
1	**Declaration Letter** From new LH/MAH Stating the ownership transfer Ensuring that there is **NO CHANGE** in product composition, specification, manufacturing process and container/closure system. The product trade Name & Reg. no. is mentioned**.** Authenticated from Chamber of commerce & Egyptian consulate/embassy + Original Arabic translation from a certified translation center.
2	**Authorization Letter** From new LH/MAH in Egypt to the current applicant. The product trade name & reg. no. is mentioned Name & address of applicant mentioned Clarifying its responsibilities for registration & all regulatory activities Authenticated from chamber of commerce & the Egyptian consulate/embassy
3	**Manufacturing contract** For UL FPP Between new LH/MAH & manufacturer. Authenticated from Chamber of Commerce, Egyptian Consulate/Embassy, EDA Legal Affairs and Bank If the contract is between the applicant & manufacturer: A letter from LH/MAH authorizing the applicant to sign contracts
4	**Packaging contract** For Bulk FPP Between new LH/MAH & packager. Authenticated from Chamber of Commerce, Egyptian Consulate/Embassy, EDA Legal Affairs and Bank If the contract is between the applicant & packager: A letter from LH/MAH authorizing the applicant to sign contracts
5	**Attached Annex** Mentioning the product name & reg. no. Authenticated from Bank & EDA Legal Affairs

Addition/Change of FPP MAH in Egypt (Imported, UL & Bulk FPP)	
1	**Declaration Letter** From LH in COO Product name, reg.no. mentioned Appointing the New MAH in Egypt clarifying its full responsibilities including but not limited to **the right to sell the product in Egypt** Authenticated from Chamber of commerce & Egyptian consulate/embassy
2	**Applicant Authorization Letter** From New MAH in Egypt Product name, reg. no. mentioned Name & address of applicant mentioned matching with Commercial Register Clarifying its responsibilities for registration & all regulatory activities Authenticated from chamber of commerce & the Egyptian consulate/embassy
3	**NO CHANGE Declaration Letter** From New MAH in Egypt Ensuring that there is **NO CHANGE** in product composition, specification, manufacturing process and container/closure system. Authenticated from chamber of commerce & the Egyptian consulate/embassy

Change/addition Supplier of solvent for a FPP (Local & UL FPP)	
1	**EDA valid registration license of solvent** If invalid: Approval for registration renewal
2	**Last Updated Commercial Register** of manufacturer of solvent
3	**Latest New Manufacturing site license** of manufacturer of solvent
4	**Letter of Variation** For UL Products From product LH in COO Stating the required variation Authenticated from chamber of commerce, Egyptian embassy/consulate or notary.

4.3.2. Quality Changes Concerning Ownership /Manufacturer variation				
4.3.2.1 Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FPP		**Requirements**		
		CADC	**Stability**	
a)	**Site where any manufacturing operation(s) take place except batch control, batch-release, Primary & secondary packaging**	***A**	****6M /None**	***** **process validation**
Condition to be fulfilled -The proposed site appropriately authorized (To perform the specified operation for the concerned FPP) -No change in FPP container closure system. -Manufacturing at the new site shall be in a compliance with cGMP if available.				
b)	**Primary packaging site.**	***A**	****6M /None**	***** **process validation**
Condition to be fulfilled -The proposed site appropriately authorized (To perform the specified operation for the concerned FPP) -No change in FPP container closure system. -Manufacturing at the new site shall be in a compliance with cGMP if available. -The change does not concern sterile FPP.				
c)	**Secondary packaging site (Non-Functional)**	**None**	**None**	**None**
Conditions to be fulfilled -The proposed site appropriately authorized (To perform the specified operation for the concerned FPP) -No change in FPP container closure system. -Manufacturing at the new site shall be in a compliance with cGMP if available.				
d)	**Batch release site**	**None**	**None**	**None**
e)	**Storage site**	**None**	**None**	**None**

Conditions to be fulfilled
-The proposed site appropriately authorized (To perform the specified operation for the concerned FPP)

Requirements guidance:

* Batch analysis for first three consecutive production batches manufactured/packed at the new site at CADC labs.

** Results of stability testing generated with a minimum of 6 months accelerated testing for first three consecutive production batches, and to be released to the market by Central Administration of Operation (Inspection Department) after evaluating the results of a minimum of 3 months of the first production batch of Finished Pharmaceutical product manufactured /packed at the new site.

Or

Evidence of no change in batch formula, description of manufacturing process, equipment class, process controls, control of critical steps & intermediates or FPP specifications.

***Process validation is performed at the new site and is followed up by EDA inspection department.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2- Relevant Documents According to Ownership & Manufacturer Variation type:

	- Replacement of a Manufacturing/Packaging site (Local & UL FPP)
1	**Cover letter on LH head letter clarifying the proposed change** Authenticated from bank
2	**Manufacturing/Packaging contract** Between LH/applicant & new manufacturer/packager, valid & authenticated from bank & EDA legal affairs. In case of a foreign party signing the contract: Authentication from chamber of commerce, Egyptian embassy/consulate or notary
3	**Attached annex of the contract** The product trade name & reg.no. is mentioned & Authenticated from bank & EDA legal affairs.
4	**Latest new manufacturing site license:** Production line &/or area needed for manufacturing the product is present.

5	**Last updated commercial register** Of the new manufacturing site
6	**If the site was previously temporarily added:** Copy of the previous approval Copies of all studies & analysis approvals done for this site.
7	**Waiver** From old manufacturing/packaging site mentioning the product name & reg. no. Stating his approval of transferring manufacturing/packaging of the product to a new manufacturing site Authenticated from bank & EDA legal affairs
8	**<u>OR</u> Termination letter** From LH to old manufacturing/packaging site signed & stamped with proof of delivery.
9	**Declaration Letter** NO change in composition, specifications, manufacturing process, or container/closure system of the FPP. *Signed & stamped.
10	**Letter of Variation** For UL Products From product LH in COO Stating the required variation Authenticated from chamber of commerce, Egyptian embassy/consulate or notary

- Addition of a Manufacturing/Packaging site (Local & UL FPP)	
1	**Cover letter on LH head letter clarifying the proposed change** Authenticated from bank
2	**Manufacturing/Packaging contract** Between LH/applicant & new Manufacturer/Packager, valid & Authenticated from bank & EDA legal affairs. In case of a foreign party signing the contract: Authentication from chamber of commerce, Egyptian embassy/consulate orNotary
3	**Attached annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from bank & EDA legal affairs
4	**Latest new manufacturing site license:** Production line &/or area needed for manufacturing the product is present.

5	**Last updated commercial register** Of the new manufacturing site
6	**If the site was previously temporarily added:** Copy of the previous approval Copies of all studies & analysis approvals done for this site.
7	**Declaration Letter** From old manufacturing/packaging site. The product trade name & reg. no. is mentioned. Stating his approval of adding a new manufacturing site. Authenticated from bank & EDA legal affairs.
8	**<u>OR</u> Declaration Letter (Template 5)** From the LH The product trade name & reg. no. is mentioned. Stating: "The company takes the full legal responsibility for adding a new site without any responsibility on EDA,regarding to the obligations and duties imposed under the manufacturing contract with the old factory (factories)".Name of old factories is mentioned". Authenticated from bank & EDA legal affairs
9	**Letter of Variation** For UL Products From product LH in COO Stating the required variation Authenticated from chamber of commerce, Egyptian embassy/consulate or notary

- Replacement or addition of a Storage Site	
1	**Cover letter on LH head letter clarifying the proposed change** Authenticated from bank
2	**Storage contract:** Between LH & storage site , valid & authenticated from bank & EDA legal affairs
3	**Storage site License**
4	**Importer record** For imported products.

- Replacement or addition of a Manufacturing/Packaging/Batch Releasing Site (Imported, UL & Bulk FPP)	
1	**Letter of Variation** From product LH in COO Product name, reg.no. mentioned Stating the required variation Authenticated from chamber of commerce, Egyptian embassy/consulate or notary.
2	**Certificate of Good Manufacturing Practice (GMP)** For new site Valid Authenticated from chamber of commerce & Egyptian consulate/embassy
3	**If the New Site is located in a non-reference country:** **CPP from Reference country:** Valid Product registered & marketed Where the proposed site in mentioned (For MFG/1ry packaging site) Authenticated by the Health Authority in COO, Chamber of commerce & Egyptian consulate

4.3.3 Change type of Registration				
4.3.3.1 change from Imported Finished to:		**Requirements**		
		CADC	**Stability**	
a)	**Bulk (for primary packaging in Egypt)**	***A**	****6M**	***** process validation**
Conditions to be fulfilled -The proposed site appropriately authorized to perform the specified operation for the concerned FPP. -The change does not concern sterile FPP.				
b)	**Bulk (for secondary packaging in Egypt)**	**None**	**None**	**None**
Conditions to be fulfilled - The proposed site appropriately authorized to perform the specified operation for the concerned FPP.				
C)	**Under license**	***A**	****6M**	***** process validation**
Conditions to be fulfilled -The proposed site appropriately authorized to manufacture product concerned.				
d)	**Local**	***A**	****6M**	***** process validation**
Conditions to be fulfilled -The proposed site appropriately authorized to manufacture product concerned. - The physical and chemical specifications must remain the same as the imported products				

Requirements guidance:

* Batch analysis for first three consecutive production batches manufactured/packed at the new site at CADC labs

** Results of stability testing generated with a minimum of 6 months accelerated testing for first three consecutive production batches, and to be released to the market by Central

Administration of Operation (Inspection Department) after evaluating the results of a minimum of 3 months of the first production batch of finished pharmaceutical product manufactured /packed at the new site.

***Process validation is performed at the new site and is followed up by EDA inspection department.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2- Relevant documents according to change type of Registration variation:

	- Change Reg. Type from Imported Finished to Imported Bulk
1	**Letter of Variation** From LH/MAH Stating the change in packaging site(s) of the product and justification for these changes The product trade name & reg. no. is mentioned Authenticated by the health authority in COO, chamber of commerce & Egyptian consulate/embassy
2	**Packaging contract** Between LH/applicant & new packager. A letter from LH/MAH authorizing the applicant to sign contracts Authenticated from bank & EDA legal affairs. Authentication form chamber of commerce, Egyptian embassy/consulate or notary is needed in case that the LH/MAH signing the contract.
3	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from bank & EDA legal affairs
4	**Latest New Packaging site license** Production line &/or area needed for manufacturing the product is present
5	**Last updated commercial register** Of the new packaging site
6	**Storage contract** Between LH/Applicant & Storage site. Valid. Authenticated from bank & EDA legal affairs. Authentication form chamber of commerce, Egyptian embassy/consulate or notary is needed in case that the LH/MAH signing the contract.

	- Change Reg. Type from Imported Finished to UL
1	**Letter of Variation** From LH/MAH Stating the change in MFG site(s) of the product and justification for these changes The product trade name & reg. no. is mentioned Authenticated by chamber of commerce & Egyptian consulate/embassy
2	**Manufacturing contract:** Between LH/Applicant & new manufacturer/packager. A letter from LH/MAH authorizing the applicant to sign contracts Authenticated from bank & EDA legal affairs. Authentication form chamber of commerce, Egyptian embassy/consulate or notary is needed in case that the LH/MAH is signing the contract.
3	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from bank & EDA legal affairs
4	**Latest new manufacturer site license:** Production line &/or area needed for manufacturing the product is present.
5	**Last updated commercial register** (New Manufacturer)
6	**Storage contract** Between LH/Applicant & Storage site.Valid. Authenticated from bank & EDA legal affairs. Authentication form chamber of commerce, Egyptian embassy/consulate or notary is needed in case that the LH/MAHsigning the contract.
7	**Submission of API supplier addition request.** Refer to API supplier addition checklist

	- Change Reg. Type from Imported Finished to Local
1	**Letter of Variation** From LH/MAH Stating the transfer of ownership of the product with clarification of the consequential changes and justification for this change The product trade name & reg. no. is mentioned Authenticated by the chamber of commerce & Egyptian consulate/embassy

2	**In case of Toll Manufacturing:** **Manufacturing contract:** Between new LH & new manufacturer/packager. Authenticated from bank & EDA legal affairs.
3	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from bank & EDA legal affairs
4	**Latest new manufacturing site license** Production line &/or area needed for manufacturing the product is present.
5	**Last updated commercial register** (New Manufacturer)
6	**Storage contract:** Between new LH & Storage site. Valid. Authenticated from bank & EDA legal affairs.
7	**Storage Site License**
8	**3 Copies Composition declaration:** **On new LH paper signed & stamped** Identical to the one attached with the registration license or to the latest finally approved composition
9	**Submission of API supplier addition request.** Refer to API supplier addition checklist

4.3.3.2 Change from Under License to:		Requirements		
a)	Imported finished	CADC	Stability	
		A*	6M**	
Conditions to be fulfilled - Satisfactory inspection in the last three years by an inspection service of a country where an operational Good Manufacturing Practice (GMP) exists. -The proposed site appropriately authorized to manufacture product concerned.				
b)	Bulk (for primary packaging in Egypt)	A*	6M**	*** process validation
Conditions to be fulfilled - Satisfactory inspection in the last three years by an inspection service of a country where an Operational Good Manufacturing Practice (GMP) exists. -The proposed site appropriately authorized to manufacture product concerned. -The change does not concern Sterile FPP.				
c)	Bulk (for secondary packaging in Egypt)	A*	6M**	
Conditions to be fulfilled - Satisfactory inspection in the last three years by an inspection service of a country where an operational Good Manufacturing Practice (GMP) exists. -The proposed site appropriately authorized to manufacture product concerned.				
d)	Local (at the same manufacturing site)	Notification	Ongoing stability study on production batches submitted upon request	
Conditions to be fulfilled - The physical and chemical specifications must remain the same as the imported product.				

e)	**Local (transfer to different manufacturing site)**	A*	**6M****	***** process validation**

Conditions to be fulfilled

-The proposed site appropriately authorized to manufacture product concerned.

- The physical and chemical specifications must remain the same as the imported product.

Requirements guidance:

* Batch analysis for first three consecutive production batches manufactured/packed at the new site at CADC labs

** Results of stability testing generated with a minimum of 6 months accelerated testing for first three consecutive production batches, and to be released to the market by Central Administration of Operation (Inspection Department) after evaluating the results of a minimum of 3 months of the first production batch of finished pharmaceutical product manufactured /packed at the new site.

***Process validation is performed at the new site and is followed up by EDA inspection department.

Submission guidance:

1-Common Administrative Documents: Refer to Annex III

(Should be submitted with all variations in addition to Relevant Documents According to the Variation Type)

2-Relevant documents according to change type of Registration variation

Change Reg. Type from UL to Imported Finished	
1	**Letter of Variation** From LH/MAH Stating the change in MFG site(s) of the product and justification for these changes.The product trade name & reg. no. is mentioned Authenticated, by chamber of commerce & Egyptian consulate/embassy
2	**Certificate of Good Manufacturing Practice (GMP)** For new MFG/Packaging site ,Valid & authenticated from chamber of commerce & Egyptian consulate/embassy
3	**Manufacturing Waiver** From old manufacturer The product trade name & reg. no. is mentioned Authenticated from bank & EDA Legal Affairs.
4	**Last Updated Importer Record**

Change Reg. Type from UL to Imported Bulk	
1	**Letter of Variation** From LH/MAH Stating the change in MFG site(s) of the product and justification for these changes.The product trade name & reg. no. is mentioned Authenticated by, chamber of commerce & Egyptian consulate/embassy
2	**Certificate of Good Manufacturing Practice (GMP)** For new MFG/Packaging site. Valid Authenticated from chamber of commerce & Egyptian consulate/embassy
3	**Manufacturing Waiver** From old manufacturer The product trade name & reg. no. is mentionedAuthenticated from Bank & EDA legal affairs
4	**Last Updated Importer Record**

Change Reg. Type from UL to Local	
1	**Letter of Variation** From LH/MAH Stating the transfer of ownership of the product with clarification of the consequential changes and justification for this change The product trade name & reg. no. is mentioned Authenticated by the chamber of commerce & Egyptian consulate/embassy
2	**Manufacturing Waiver** From old manufacturer (In case of changing MFG site) The product trade name & reg. no. is mentioned Authenticated from Bank & EDA legal affairs
3	**In case of Toll Manufacturing:** **Manufacturing contract:** Between new LH & new manufacturer/packager. Authenticated from bank & EDA legal affairs.
4	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from bank & EDA legal affairs

5	**Latest New Manufacturing site license** Production line &/or area needed for manufacturing the product is present.
6	**Storage contract:** Between new LH & Storage site. Valid. Authenticated from bank & EDA legal affairs.
7	**Storage Site License**
8	**Copies Composition declaration**: On new LH Paper Signed & stamped Identical to the one attached with the registration license or to the latest finally approved composition

5. Annexes:

Annex I: Glossary

EDA	Egyptian Drug authority
FPP	Finished Pharmaceutical Product
CPP	Certificate of pharmaceutical products
cGMP	Current Good Manufacturing Practice
COA	Certificate of Analysis
NRA	National Regulatory Authority
SRAs	Stringent regulatory authorities
LH	License holder
MAH	Marketing Authorization Holder
CADC	Central Administration of Drug Control
API	Active Pharmaceutical Ingredient

Annex II: EDA's approved list of reference countries.

The current list consists of 22 countries

- Australia
- United States of America
- Austria
- Belgium
- Norway
- Canada
- Sweden
- Denmark
- Finland
- France
- Switzerland
- United Kingdom
- Germany
- Iceland
- Ireland
- Italy
- Portugal
- Spain
- Luxembourg
- Netherland
- New Zealand
- Japan

Annex III: Common Administrative Documents:

Should be submitted with all variations in addition to Relevant Documents According to the Variation Type

Section (1)	
Variation Application form (Signed and Stamped) + Payment receipt	
Required Documents	
1	Variation Application form (Template1)
2	Payment receipt
Section (2)	
EDA License & Approvals	
Required Documents	
1	**EDA Valid Registration License** - If invalid: valid Approval for registration or prove of submission for reregistration
2	Any other EDA or Variation approvals.
3	Any Previous Stability Approvals (Accelerated Stability or Long-term Stability).
4	EDA labs certificate of analysis.
5	EDA labs composition certificate.
Section (3) **Other Documents (In Case of Imported / UL Products)**	
Required Documents	
1	**Valid CPP/e CPP (With All Attachment)** Authenticated by the Health Authority in country of origin, Chamber of commerce & Egyptian consulate/embassy.
2	**Declaration Letter from LH/MAH in country of origin** - Clarifies the change if not stated in CPP & Stating the reasons of change
Section (4)	
Applicant Documents	
Required Documents	
1	Last Updated Commercial Register
2	Toll Card In case of toll companies
3	Factory License In case of local companies
4	Scientific office License In case of scientific office
5	In Case of Imported finished veterinary Pharmaceutical Product if the applicant is either Scientific Office or Company the following documents to be submitted: -

	Scientific Office: a) Authorization letter for the scientific office to register finished Imported veterinary Pharmaceutical Products" issued by inquiry requests unit for veterinary pharmaceuticals. b) Declarations Letter Clarifying the Company's profile Code signed & stamped **Company:** Declarations Letter Clarifying the Company's profile Code describing its activity as "Company Authorized for Registration" And if not Available The company must apply to systems & information unit for creating a company profile to be able to submit variation requests

Annex IV: Final approvals submission guidance:

Section (1)
1- Latest issued EDA registration license
2- Variation Application Form of Post Marketed Veterinary Products (Template 1)

Section (2)	
Composition variation final approval	
1	A copy of primary approval
2	All Studies issued on primary approval for the product and its original copies (to be seen): a) EDA Labs COA & Composition b) Stability Approval
3	Approved Composition "on company paper signed and stamped".
Pack variation final approval	
1	A copy of primary approval
2	All Studies issued on primary approval for the product and its original copies (to be seen): a) EDA Labs COA & Composition b) Stability Approval
API manufacturer variation final approval	
1	A copy of primary approval
2	All Studies issued on primary approval for the product and its original copies (to be seen): a) EDA Labs COA & Composition b) Stability Approval

Annex V: Updating analysis file submission guidance

1-Common Administrative Documents: Refer to Annex III

2- Relevant Documents:

1	Composition "on company paper signed and stamped".
2	CADC Labs Analysis Certificate **Or** A "Not Found" Letter from CADC
3	CADC Labs Composition **Or** A "Not Found" Letter from CADC

6. Templates
6.1 Template 1
Variation Application Form of post Marketed Veterinary Products

Name of the product/s:	**Applicant:**
Active substance(s):	**Manufacturer of Finished Pharmaceutical product:**
Concentration:	**Manufacturer of solvent:**
Dosage form:	**Name of contact:**
Registration number:	**Telephone number:**
E-mail:	

Variation changes (Tick the appropriate change required) **Please Tick all the variations submitted in case of multiple variations**	**Change**	**Addition**	**Clarify**
A) Composition & Specification Changes As:			
Name of active substance			
Name of an Excipient			
Excipient			
Changes in components of the flavoring or coloring system			
Specification of Active ingredient			
Specification of Inactive ingredients			
API form as salt equivalence and/or crystalline state			
The particle size of API (state D90)			
Addition of an overage			
Tightening of Specification limits			
Deletion of a non-significant specification parameter			
Widening of specification limits			
Change the Pharmacopeial product			
Shelf life			
Storage Conditions			
Change in range of color			
Scoring			

	Change	Addition	Clarify
B) Container Closure System Changes As:			
Primary packaging of finished pharmaceutical product			
Pack size of finished pharmaceutical product			
Change in shape or dimensions of the container or closure (immediate packaging)			
Part of primary packaging material not in contact with the finished product formulation			
C) API Manufacturer changes as:			
Name of API Manufacturer			
Address of API Manufacturer			
Deletion of API Manufacturer			
API Manufacturer			
D) Ownership / Manufacturer Changes As:			
Name of License holder			
Address of License holder			
Name of Manufacturing site			
Address of Manufacturing site			
Applicant for imported FPPs			
Modification of Registration License			
License Holder Transfer			
Marketing Authorization holder Transfer			
Marketing Authorization holder in **Egypt**			
Solvent Manufacturer			
Manufacture site			
Primary Packager			
Batch releasing site of FPP			
Storage Site			
Change Registration Type			
E) Miscellaneous			**Tick for requiredIssue**
Updating Analysis File			
Final Approval for Composition/Specification			
Final Approval for Pack			
Final Approval for API			
Appeal			
Cancelling previous variation approvals			
F) others			

BACKGROUND & JUSTIFICATION FOR REQUIRED CHANGE/S **(Please give brief background explanation for the proposed changes)**	
Current	**Proposed**
In case of Appeal / Final Approvals: (Please Clarify exactly the issue required)	
The applicant is committed to the following	**Yes**
1- All documents & information submitted in the file are correct and on the responsibility of the company	
2- The submitted file contains all the approvals for the product that were not mentioned in the last released registration license	
3- The submitted file contains the latest issued registration license	
4- The submitted file contains all approvals, variations & decisions issued for the product from different EDA departments	
Kindly state the following data:	
1- In case of Any previous variations' approvals, variations & decisions issued for the product fromdifferent EDA departments **(please arrange the with dates if available)**	
1- 2-	
2- Data of the last manufactured/imported production batch:	
A- Batch No.: B- Production date: C- Expiry date:	
3- Payment receipt No: (Its Value according to Variation Request, must be directed to variation department and stamped with EDA Stamp with the Product Name, Concentration, Dosage Form, Typeof variation.	
Signature by the Authorized Person:	**Company Stamp:**

6.2 Template 2

(API Variation Notification Form)

السيد الدكتور / رئيس الادارة المركزية للمستحضرات الصيدلية
الإدارة العامة للمستحضرات البيطرية
إدارة المتغيرات

Product Name:	
Dosage Form:	
Reg. No.:	
License Holder:	
Manufacturer:	

Current API(s) Manufacturer (s):	**Proposed API (s) Manufacturer(s):**
1-	**1-** **Address:**
2-	**2-** **Address:**
3-	**3-** **Address:**
4-	**4-** **Address:**

تتعهد الشركة بتقديم الـ GMP وشهادات التحليل الخاصة بالمادة الخام وذلك عند التقدم لإستيراد المادة الخام بهيئة الدواء المصرية.

و تفضلوا بقبول وافر الإحترام والتقدير

رئيس مجلس ادارة الشركة **ختم الشركة**

6.3 Template 3

السيد الدكتور / رئيس الإدارة المركزية للمستحضرات الصيدلية
الإدارة العامة للمستحضرات البيطرية
إدارة المتغيرات

تحية طيبة وبعد

أتعهد أنا ..... رئيس مجلس إدارة شركة ..... بأن المستحضرات المملوكة للشركة التي تحتوي علي نفس المواد الفعالة هم كالأتي:

Registered Product		Under-Registration Products	
Trade Name / Dosage Form	**API/Strength**	**Trade Name / Dosage Form**	**API/Strength**

و تفضلوا بقبول وافر الإحترام والتقدير

رئيس مجلس ادارة الشركة **ختم الشركة**

6.4 Template 4

السيد الدكتور / رئيس الإدارة المركزية للمستحضرات الصيدلية
الإدارة العامة للمستحضرات البيطرية
إدارة المتغيرات

تحية طيبة وبعد

أتعهد أنا ..... رئيس مجلس إدارة شركة ..... بأن المستحضرات المملوكة للشركة هم كالأتي:

Registered Product		Under-Registration Products	
Trade Name / Dosage Form	**API/Strength**	**Trade Name / Dosage Form**	**API/Strength**

و تفضلوا بقبول وافر الإحترام والتقدير

رئيس مجلس ادارة الشركة **ختم الشركة**

6.5 Template 5

السيد الدكتور / رئيس الإدارة المركزية للمستحضرات الصيدلية
الإدارة العامة للمستحضرات البيطرية
إدارة المتغيرات

تحية طيبة وبعد

بخصوص المستحضر البيطري الأتي:

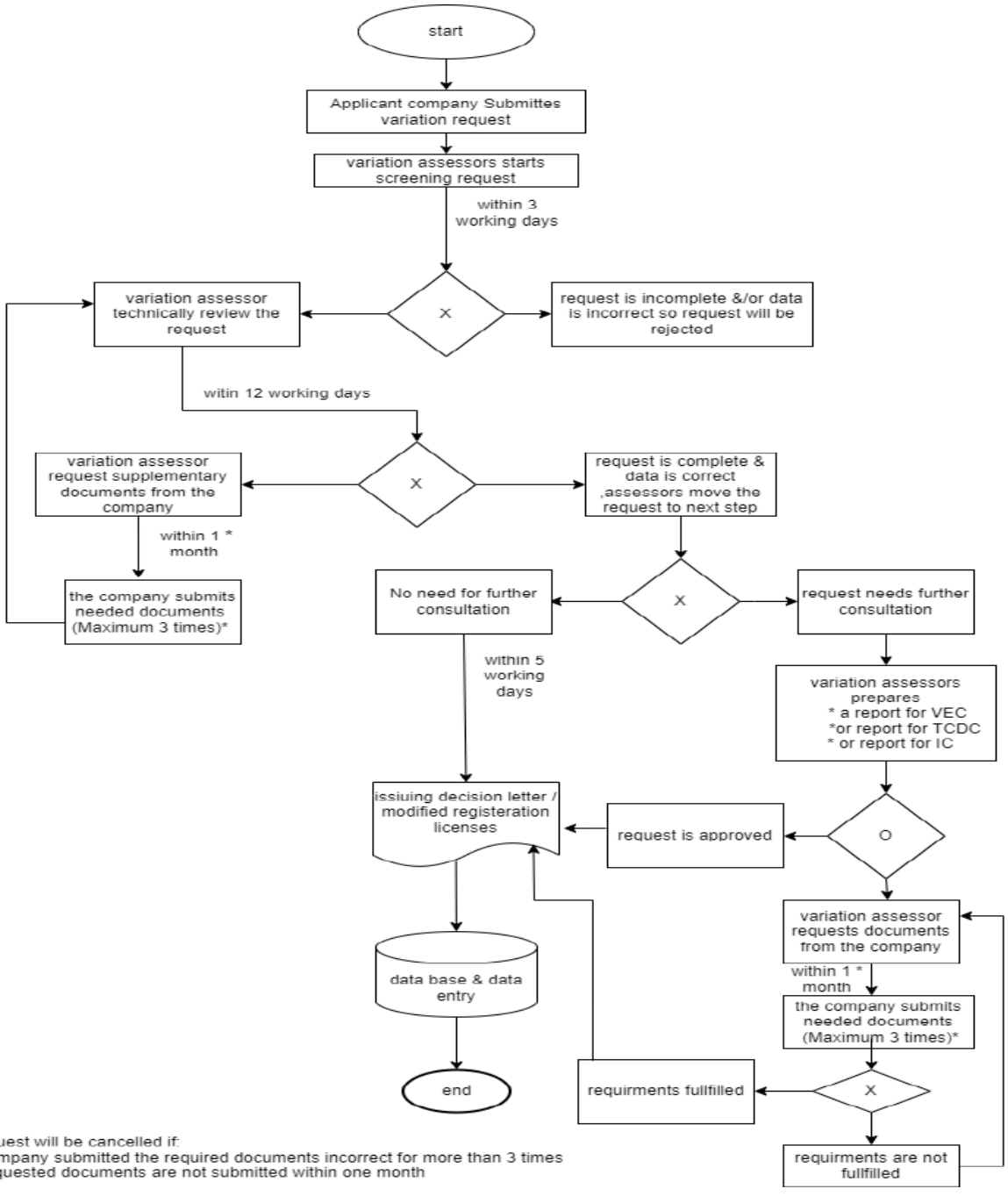
Trade Name:	
Dosage Form:	
Active Ingredients / Strength:	
Registration No.:	
Applicant Company:	
License Holder / MAH:	
Manufacturer:	

أتعهد أنا ..... رئيس مجلس إدارة شركة ..... بتحمل كافة المسؤولية القانونية لإضافة مكان التصنيع .....(اسم المصنع الجديد/المصانع الجديد) دون أدنى مسؤولية على هيئة الدواء المصرية تجاه عقود التصنيع المبرمة بين شركة .....(اسم المالك للمستحضر) وشركة .....(اسم المصنع القديم/المصانع القديمة)

و تفضلوا بقبول وافر الإحترام والتقدير

رئيس مجلس ادارة الشركة **ختم الشركة**

7-Variation Flow Chart:



Note :
The request will be cancelled if:
*The company submitted the required documents incorrect for more than 3 times
*The requested documents are not submitted within one month

8. References:

- **Guidance from the European Medicines Agency (EMA) on variations for centrally authorized veterinary medicines not requiring assessment under the Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6) dated on 8 January 2021.**

- **Guidance from the European Medicines Agency (EMA) on variations for centrally authorized veterinary medicines requiring assessment under the Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6) . Last updated on 25/4/2023**

- **WHO guidelines on variations to a prequalified product (Annex III).**

- **Egyptian Variation Guidelines Second Edition 2019.**

-**Technical Committee of Drug Control relevant decisions**.