Notice to applicant

Central Administration of Pharmaceutical Products

General Administration For Human Pharmaceutical Products

Administrative, Relevant Documents &Time frame for human pharmaceutical variations

Year 2026

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I) Introduction:

- These Documents have been developed to provide a standardized, clear and efficient approach for applicants preparing a Common Technical Document for submission a Variation of Pharmaceutical products.
- The purpose of these Documents is to outline the required documentations which have to be generated in case of all submitted variation requests in align with Sixth edition guidelines on human pharmaceutical variations.
- The applicant submits Variation Requests to notify EDA that it will carry out a new variation with full company responsibility for conducting all required supporting studies concerning the variation (Variation Inquiry without Assessment) or to notify EDA that it will carry out a new variation with requesting which studies should be fulfilled for this variation (Variation Inquiry with Assessment) or submit all required studies and/or supporting documentation, along with their corresponding approvals issued by the relevant EDA administrations for the requested variation (Post-Marketing Variation Approval)
- Common Administrative Documents Should be submitted with all variations in one folder in addition to Relevant Documents in another separate folder According to the Variation Type
- The Working days for fulfilled variation requests as the following:

1	**Human Pharmaceutical Variation Inquiry with assessment**	**45 W.D.**
2	**Human Pharmaceutical Variation Appeals**	**45 W.D.**
3	**Human Pharmaceutical Variation Inquiry without assessment**	**15 W.D.**
4	**Human Pharmaceutical Post Marketing Variation Approvals**	**60 W.D.**
5	**Human Pharmaceutical Variation Approvals according to Reliance pathway**	**45 W.D.**

* In case of typing error, Variation Specialist Assessor re-edits registration license, notification, acceptance, or rejection letters **within 15 working days**.

II) Common Administrative Documents:

Section (1) Variation Application form (Signed and Stamped) + Payment Receipt	
1	**Variation Application form*.** Signed and stamped
2	**Payment Receipt.**

Section (2) EDA License & Approvals	
1	**EDA Valid Registration License** ▪ If Final & invalid: Valid Approval for registration renewal. ▪ If Tentative & invalid: License validity extension approval or approval for submission from Tent. to final.
2	Any other EDA or Variation approvals or any Exemptions for the product.
3	Minister decree 600 exemption (If needed).
4	Any Previous Stability Approvals (Accelerated Stability or Long-term Stability).
5	Leaflet of the product and innovator.
6	EDA labs certificate of analysis.
7	EDA labs composition certificate.

8	Updated Pricing License

Section (3) **Other Documents (In Case of Imported / UL Products)**	
1	▪ **Valid CPP (With All Attachment):** Authenticated by the Health Authority in COO, Chamber of commerce or Notary & Egyptian consulate/embassy. **OR** ▪ **Electronic CPP** & Declaration Letter from The Applicant Clarifies the Authorized Link for its **Online Verification**
2	**Declaration Letter from LH/MAH in COO** ▪ Clarifies The Changes. if The Change(s) **stated in The CPP** The Declaration Should be Signed and stamped & if The Change(s) **doesn't stated in The CPP** (for 2ry Packager / Batch Release Site), The Declaration Letter should be **Authenticated** from Chamber of commerce or Notary & Egyptian consulate/embassy.
3	**Declaration Letter from LH/MAH in COO signed and stamped**: ▪ Stating the reasons of change.
4	**CTD:** ▪ Part related to required change.

Section (4) **Applicant Documents**	
1	**Last Updated Commercial Register**

2	**Last Updated Toll Card** ***** In case of toll companies
3	**Last Updated Manufacturing License** ***** In case of local companies
4	**Scientific Office License** *****In case of scientific office
5	**In Case of Imported Finished Human Pharmaceutical Product if the applicant is either Scientific Office or Company the following documents to be submit:** ***Scientific Office:** **a) "Authorization letter for the Scientific Office to register finished Imported Human Pharmaceutical Products"** issued by Evaluation Unit of registration requests for human 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 **N.B.: If Applicant Change for the Imported finished Pharmaceutical Product is needed** kindly submit separate Fulfilled file (as check list) for the Applicant change

III) Relevant Documents According to the Variation Type:
(section 5):

5.1. Change in Name / Address of Finished product LH/MAH	
A- For Local FPP	
1	**Fees:** 1000 L.E.
2	**Last Updated Commercial Register of The Company.** Mentions the **New** Name of The Company.
3	**Declaration Letter** With list of all products affected by this name change. *Signed & stamped.
4	**Declaration Letter** The proposed company trade name in English *Signed & stamped.
B- For Imported, UL & Bulk FPP	
1	**Fees:** 1000 L.E
2	**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 or Notary & Egyptian consulate/embassy

5.2. Change in name of the Active Substance or of an excipient	
1	**Fees:** 1000 L.E.
2	Old composition "signed and stamped".
3	New composition "signed and stamped".
4	Comparison table between old and new composition.
5	C.O.A of all suppliers of Active / inactive Ingredients.
6	Pharmacopeia Monograph active ingredient or reference for the name of inactive ingredient.
7	All updated relevant sections of the CTD part related to the new change.

5.3. Change in the name and /or address of: a manufacturer of the active substance / starting material, reagent or intermediate used in the manufacture of the active substance.	
1	**Fees:** 1000 L.E.
2	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 Imported Finished / Bulk pharmaceutical product, Quality module 3 (S-Part) 3.2.S.2.1 section can be submitted in case of GMP is not available. **In case of new name certificate is not including API:** Complete & recent API manufacturer license (or CPP for Korea) with the same new name certificate address & mentioning the API(s) name.
3	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.
4	**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 the API production line.
5	**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).
6	**In case of different addresses between the old & new names API manufacturer(s) certificates without change in location:** Letter of authority which is responsible for the manufacturer inspection mentioning that the change in address is administrative. Declaration letter from API manufacturer mentioning that API supplied from old address, if new extensions are not for API supply Layout for the API manufacturer clarifying the entrances of the manufacturer, if the manufacturer has two entrances.
7	All updated relevant sections of the CTD part related to the new change.

5.4. Deletion of manufacturing sites for an active substance, intermediate or finished product, packaging site, manufacturer responsible for Batch Releasing Site, Batch control Site, storage site
5.4.a. Deletion of manufacturing sites for an active substance

1	**Fees:** 1000 L.E.
2	For API manufacturer(s) that will be authorized for API manufacturing**, submit one of the following (In case of address is not mentioned in any previous approvals and/ or Marketing Authorization):** ▪ GMP. ▪ ISO 9001 – 2015 (for Minerals, Vitamins and Extracts only). ▪ CPP. ▪ Written confirmation letter. **In addition to** Invoices stating API manufacturer address Stamped from Directorate of Importation and customs release of pharmaceutical raw material and /or importation approvals and/or production plans and/or withdrawal report with Studies are required to be submitted.
3	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 the API production line.
4	All updated relevant sections of the CTD part related to the new change.

5.4.b. Deletion of a Manufacturing/Packaging site/ Batch Releasing Site	
	A- For Local FPP
1	**Fees:** 1000 L.E
2	**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

	OR **Termination letter** From LH to Old Manufacturing/Packaging Site signed & Stamped With proof of delivery.
	B- (Imported/UL / Bulk Products)
1	**Fees:** 1000 L.E
2	**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
3	**For UL/Bulk FPP** **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 **OR** **Termination letter** From LH to Old Manufacturing/Packaging Site signed & Stamped

	With proof of delivery.

5.5. Change in Name / Address of Manufacturing sites	
	A- For Local FPP
1	**Fees:** 1000 L.E.
2	**Last Updated Factory License** **Released from EDA** "Stating the New Name of the Manufacturing site"
3	**Declaration Letter** With list of all products affected by this name change. *Signed & stamped.
	B- For Imported, UL & Bulk FPP
1	**Fees:** 1000 L.E.
2	**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 or Notary & Egyptian consulate/embassy
3	**Certificate of Good Manufacturing Practice (GMP)** For the Site with the **NEW** Name/Address

	Valid Authenticated from Chamber of commerce or Notary & Egyptian consulate/embassy
4	**Certificate of Good Manufacturing Practice (GMP)** For the Site with the **OLD** Name/Address Authenticated from Chamber of commerce or Notary & Egyptian consulate/embassy (If applicable)
5	**Official document from a relevant official body** In case of changing address Justifying the change in address

5.6. Change in Applicant for Registration (Imported, UL & Bulk FPP)	
1	**Fees for Imported FPP:** ▪ In Case of Transfer from Scientific office to Company: 6000 L.E. ▪ In Case of Transfer from Company to Scientific Office: 16000 LE. ▪ In Case of Transfer from Scientific Office to Scientific Office: 11000 LE. **Fees For UL & Bulk FPP:** 1000 L.E.
2	**In Case of Imported Finished Human 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 Human Pharmaceutical Products"** issued by Evaluation Unit of registration requests for human 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 **N.B.: If Applicant Change for the Imported Finished Pharmaceutical Product is needed** kindly submit separate Fulfilled file (as check list) for the Applicant change**.**
3	**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 **Or Waiver** From Old Applicant The product trade name & reg. no. is mentioned Authenticated from Bank
4	**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 or Notary & the Egyptian consulate/embassy **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 or Notary & the Egyptian consulate/embassy
5	**Commercial Register** for Old Applicant **OR** **Scientific Office License for old applicant** In case of scientific office
6	**For UL FPP** **Manufacturing contract** Between New Applicant & Manufacturer. Authenticated from Chamber of Commerce, Egyptian Consulate/Embassy, EDA Legal Affairs and Bank
7	**Attached Annex** Mentioning the product name & reg. no.

5.7. Modification of Registration License	
1	**Fees:** 1000 L.E.

2	**EDA Approval** Of the required change to be updated in the registration license issued from relevant EDA department

	5.8. Finished product License Holder
	A- For Local FPP
1	**Fees:** 5000 L.E.
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 New 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	**3 Copies Composition declaration** On New LH head letter Identical to the one attached with the registration license or to the latest finally approved composition

	Signed & stamped
6	**Declaration Letter (Template 1)** From Old LH FPP does not have any other strengths of the same dosage form or other dosage forms either registered or under registered products. Signed & stamped.
7	**Declaration Letter (Template 2)** From New LH FPP does not have any other strengths of the same dosage form or other dosage forms either registered or under registered products. Signed & stamped.
8	**Declaration Letter (Template 3)** Stating all registered & under-registrations human FPP with their active ingredients owned by the new License Holder In case of Toll companies Signed & stamped.
9	**Declaration Letter** The new LH is committed to provide all safety data related to the product since its placement in market - when needed in addition to implementing all its vigilance activities.
10	**1st Marketing Permission Report** For the products registered under the ministerial decree 425/2015 & 645/2018.
	B- For Imported/ UL / Bulk Products

1	**Fees:** 5000 L.E.
2	**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 or Notary & Egyptian consulate/embassy
3	**Authorization Letter** From New LH 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 or Notary & the Egyptian consulate/embassy
4	**For UL FPP** **Manufacturing contract** 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**

5	**<u>For Bulk FPP</u>** **Packaging contract** Between New LH/MAH & Packager. Authenticated from Chamber of Commerce, Egyptian Consulate/Embassy, EDA Legal Affairs and Bank ***<u>If the contract is between the applicant & packager:</u>** A letter from LH/MAH authorizing the applicant to sign contracts
6	**Attached Annex** Mentioning the product name & reg. no. Authenticated from Bank & EDA Legal Affairs

5.9. Addition/Change of FPP MAH in Egypt (Imported/ UL / Bulk Products)	
1	**Fees:** 5000 L.E.
2	**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
3	**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
4	**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

5.10. Addition/Change of Marketing Rights Holder of Finished Product (For Local Products)	
1	**Fees:** 5000 L.E. / Country
2	**Marketing Agreements** Between New LH/MAH & Marketing Rights Holder Valid Authenticated from Bank & EDA Legal Affairs
3	**Attached Annex** Mentioning the product name & reg. no. Authenticated from Bank & EDA Legal Affairs

5.11. Change/addition Solvent / Diluent manufacturer supplied for a FPP (Local / UL Products)

1	**Fees:** 1000 L.E.
2	**EDA Valid Registration License of solvent** If Final & invalid: Approval for registration renewal If Tentative & invalid: License validity extension approval or approval for submission from Tent. To final
3	**In Case of Lidocaine Addition/Change:** Composition of Lidocaine from the old and new Supplier Previously approved stability study and AR for the old lidocaine Supplier
4	**Declaration Letter:** Of The Pack Type of solvent from the OLD supplier.
5	**For UL FPP** **Letter of Variation** From product LH in COO Stating the required variation Authenticated from chamber of commerce, Egyptian embassy/consulate or Notary

5.12. Addition / Change in the manufacturer	
Fees: 1000 L.E.	
A.	**Addition or replacement of a new manufacturer for intermediate / starting material:**
1	Commitment from API manufacturer, where applicable that the starting material specifications and analytical procedures and the active substance & intermediate (used in the manufacturing process of the

	active substance) synthetic route, quality control procedures and specifications are the same as those already approved.
2	Where relevant, a commitment of the manufacturer of the active substance to inform the marketing authorization holder of any changes to the manufacturing process, specifications and analytical procedures of the active substance.
3	All updated relevant sections of the CTD part related to the new change.
B.	**Change in manufacturer of the active substance**
B.1.	**Addition or replacement of a new manufacturer for API:**
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 for Korea) with the same address of GMP certificate & mentioning the API(s) name.
2	**For the current API manufacturer(s), 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 mention the API(s) manufacturer name & its address.
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 the API production line.
4	**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. Particle size test range in numbers & solubility test are required if the API particle size will be changes or clarified in the Product Registration License Composition
5	**In case of the submitted CoA on manufacturer letterhead Different from the API manufacturer:** Relationship Declaration Letter between the two manufacturers is required.
6	Updated Pharmacopeia Monograph for API(s).
7	**In case of API is Pellets/Premix/Granules:** Composition on API manufacturer letterhead & matching with Product Registration License Composition
8	**In case of Pellets specification is <u>not In-house</u>:** Justification on API manufacturer letterhead.
9	All updated relevant sections of the CTD part related to the new change.
B.2.	**Changes to quality control testing arrangements for the active substance-replacement or addition of a site where batch control/testing takes place:**
1	Amendment of the relevant section(s) of the dossier.
2	Valid proof that the proposed site is GMP compliant for the testing operations.
3	Certificate of analysis.
B.3.	**Addition or replacement of a new site of micronization of the active substance:**
1	Amendment of the relevant section(s) of the dossier.

2	Certificate of analysis
3	All updated relevant sections of the CTD part related to the new change.

5.13. Changes in the manufacturing process of the active substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	Certificate of analysis
4	Copy of approved specifications of the active substance.
5	All updated relevant sections of the CTD part related to the new change.

5.14. Change in batch size of active substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	Certificate of analysis
4	All updated relevant sections of the CTD part related to the new change.

5.15. Change to in-process tests or limits applied during the manufacture of the active substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.

3	Comparative table of current & proposed in-process control & limits.
4	Details of any new non-pharmacopeial analytical method and validation data, where relevant
5	Certificate of analysis.
6	Justification from the API manufacturer as appropriate for the new in-process control and limits
7	All updated relevant sections of the CTD part related to the new change.

5.16. Change in the specification parameters and/or limits of an active substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	COAs for current and proposed changes.
4	Comparative table of current & proposed specifications.
5	Justification from the API manufacturer as appropriate of the new specification attribute and the acceptance criteria.
6	Details of any new analytical procedure and validation data, where relevant.
7	All updated relevant sections of the CTD part related to the new change.

5.17. Change to analytical procedure for active substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier, including a description of the analytical methodology, a summary of validation data, revised specifications.
3	Comparative validation results, or if justified comparative analysis results showing that the current analytical procedure and the proposed one are equivalent. This requirement is not applicable in case of

	an addition of a new analytical procedure unless the new analytical procedure is added as an alternative procedure to a current on
4	All updated relevant sections of the CTD part related to the new change.

5.18. Change in immediate packaging of the active Substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	Comparison between current & proposed immediate packaging specifications of active substance, if applicable.
4	The results of stability study of a new immediate packaging material from API manufacturer.
5	All updated relevant sections of the CTD part related to the new change.

5.19. Change in specification or acceptance criteria of immediate packaging of the active Substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	Comparative table current & proposed specifications of immediate packaging of active substance.
4	Justification from the API manufacturer as appropriate, of the new specification attribute and the acceptance criteria.
5	All updated relevant sections of the CTD part related to the new change.

5.20. Change in analytical procedure for immediate packaging of the active Substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier, including a description of the analytical methodology, a summary of validation data
3	Comparative validation results or if justified comparative analysis results showing that the current analytical procedure and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new analytical procedure.
4	All updated relevant sections of the CTD part related to the new change.

5.21. Change in the retest period/storage period or storage conditions of the active substance	
Fees: 1000 L.E.	
a) Retest period / storage period:	
1. Reduction	
1	Amendment of the relevant section(s) of the dossier.
2	Results of stability study of API manufacturer for proposed.
3	Justification for proposed
4	Copy of approved specifications for proposed.
5	All updated relevant sections of the CTD part related to the new change.
2. Extension or introduction of a retest period / storage period supported by real time data.	
1	Comparison between current & proposed changes.
2	Results of stability study from API Manufacturer.

3	All updated relevant sections of the CTD part related to the new change.
b) Storage conditions:	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	Results of stability study from API Manufacturer.
4	Justification for proposed
5	Copy of approved specifications of the active substance.
6	All updated relevant sections of the CTD part related to the new change.
c) Change to approved Stability Protocol:	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	Copy of approved specifications of active substance.
4	All updated relevant sections of the CTD part related to the new change.

5.22. Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability for an active substance	
Fees: 1000 L.E.	
a.	**New certificate from an approved manufacturer**
b.	**Updated certificate from an already approved manufacturer**
1	Amendment of the relevant section(s) of the dossier.

2	Comparison between current & proposed changes.
3	Copy of the current and/or updated Ph. Eur. certificate of suitability (CEP) and the letter of access (where available).
4	All updated relevant sections of the CTD part related to the new change.
c.	**New certificate for a non-sterile active substance that is to be used in a sterile medicinal product, where water is used in the last steps of the synthesis and the material is not claimed to be endotoxin free**
1	Amendment of the relevant section(s) of the dossier.
2	Comparison between current & proposed changes.
3	Copy of the current and/or updated Ph. Eur. certificate of suitability (CEP) and the letter of access (where available).
4	Copy of the current and/or updated Ph. Eur. certificate of suitability (CEP) and the letter of access (where available). Suitable evidence to confirm compliance of either the water used in the final steps of the synthesis of the active substance, or the active substance, itself with the corresponding requirements of the guideline on quality of water for pharmaceutical use regarding bacterial endotoxins and microbiological quality.
5	All updated relevant sections of the CTD part related to the new change.

❖ **In case of current API manufacturer address is not mentioned, Invoices Stamped from Directorate of Importation and customs release of pharmaceutical raw material / importation approvals / production plans / withdrawal / Studies are required to be submitted.**

5.23. Change or addition of imprints, bossing (embossing/debossing) or other markings including replacement, or addition of inks used for product marking

1	**Fees:** 1000 L.E.
2	Old composition "signed and stamped". (If needed)
3	New composition "signed and stamped". (If needed)
4	Safety Data Sheet for Ink including composition of ink (In case of change or addition of imprints).
5	Reference for scoring (In case of Change or addition of scoring/break lines on tablets).
6	Commitment to be written in pamphlet and on outer pack, reference of Innovator and its leaflet (In case of Addition of Non-Functional Scoring / break lines).
7	Commitment that change doesn't affect on stability of the product.
8	All updated relevant sections of the CTD part related to the new change.

5.24. Change in the shape or dimensions of the pharmaceutical form	
1	**Fees:** 1000 L.E.
2	Sample (IF Needed).
3	Old & New Certificate of Analysis.
4	Old & New finished Pharmaceutical product specifications.
5	Commitment that change doesn't affect on stability of the product.
6	All updated relevant sections of the CTD part related to the new change.

5.25. Changes in the composition (excipients) of the finished pharmaceutical product	
1	**Fees:** 1000 L.E.

2	Old composition "signed and stamped".
3	New composition "signed and stamped".
4	Comparison table between old and new composition.
5	In case of hard gelatin capsule: submit capsule shell composition on supplier paper.
6	In case of clarification of capsule shell composition: A report from Inspection Department stating the Capsule shell composition including batch record if not documented in any previous approvals.
7	In case of Coating blends (e.g. Opadry / Eudragit / Kollicoat / Flavors on supplier paper/ Ink), submit composition and COA of supplier.
8	Scientific justification & Reference and write in composition the cause of Addition (e.g. for Manufacturing loss) (In case of Elimination, Reduction or Addition of an overage (Flow chart needed in case of overage).
9	C.O.A & Composition of all suppliers of Active Ingredient or Premixes.
10	Calculations of pellets/Premix on applicant paper head.
11	In Case of Change of salt equivalence and/or crystalline state of the drug substance (refer to section 5.11).
12	Scientific Reference for Finished Pharmaceutical Product PH (In Case of Change PH Range).
13	Calculation of approved limit (In case of presence of Methyl paraben and propyl paraben in oral liquid dosage forms 'suspension and syrup').
14	All updated relevant sections of the CTD part related to the new change.

	5.26. Change in coating weight of oral dosage forms or change in weight of capsule shell
1	**Fees:** 1000 L.E.
2	Old composition "signed and stamped".
3	New composition "signed and stamped".

4	Comparison table between old and new composition.
5	In case of hard gelatin capsule: submit capsule shell composition on supplier paper.
6	In case of Coating blends (e.g. Opadry / Eudragit / Kollicoat / Flavors on supplier paper/ Ink), submit composition and COA of supplier.
7	Scientific justification & Reference and write in composition the cause of Addition (e.g. for Manufacturing loss) (In case of Elimination, Reduction or Addition of an overage).
8	Commitment that Finished Pharmaceutical product specification has only been updated in respect of weight and dimensions.
9	All updated relevant sections of the CTD part related to the new change.

5.27. Change in the manufacturing site for part or all of the manufacturing process of the finished product	
5.27.1. Replacement of a Manufacturing/Packaging Site (Local / UL Products)	
1	**Fees:** 1st site: 3000 L.E 2nd site: 5000 L.E 3rd site: 10000 L.E 4th site: 20000 L.E **N.B: For Transferring the storage site refer to the fees of storage site transfer**
2	**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 **<u>OR</u> Termination letter** From LH to Old Manufacturing/Packaging Site signed & Stamped With proof of delivery.
3	**Manufacturing/Packaging contract** Between LH/Applicant & New Manufacturer/Packager. Valid. Authenticated from Bank & EDA Legal Affairs. ***If the contract is between the applicant & Manufacturing/Packaging site:** A letter from LH/MAH authorizing the applicant to sign contracts Authenticated from chamber of commerce or Notary& Egyptian embassy/consulate
4	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
5	**Last Updated Manufacturing site license:** Production line &/or area needed for manufacturing the product is present.
6`	**Last Updated Commercial Register** Of the new manufacturing site
7	**If the site was previously temporarily added:** Copy of the previous approval

	Copies of all studies & analysis approvals done for this site.
8	**<u>For UL FPP</u>** **Letter of Variation** From product LH in COO Stating the required variation Authenticated from chamber of commerce, Egyptian embassy/consulate or Notary
9	**<u>For Toll Companies</u>** Last Valid Updated Toll Card /Annex including the requested Manufacturing/ Packaging site

5.27.2. Addition of a Manufacturing/Packaging site (Local / UL Products)	
1	**Fees:** 2nd site: 5000 L.E 3rd site: 10000 L.E 4th site: 20000 L.E **N.B: For addition the storage site refer to the fees of storage site addition**
2	**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. **<u>OR</u> Declaration Letter (Templet 4)**

	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.
3	**Manufacturing/Packaging contract** Between LH/Applicant & New Manufacturer/Packager. Valid. Authenticated from Bank & EDA Legal Affairs. ***If the contract is between the applicant & Manufacturing/Packaging site: A letter from LH/MAH authorizing the applicant to sign contracts** **Authenticated from chamber of commerce or Notary& Egyptian embassy/consulate**
4	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
5	**Last Updated Manufacturing site license:** Production line &/or area needed for manufacturing the product is present.
6	**Last Updated Commercial Register** Of the new manufacturing site
7	**In case of Tentative registration license:**

	AR approval of the 1st production batch from CADC
8	**If the site was previously temporarily added:** Copy of the previous approval Copies of all studies & analysis approvals done for this site.
9	**<u>For UL FPP</u>** **Letter of Variation** From product LH in COO Stating the required variation Authenticated from chamber of commerce or Notary& Egyptian embassy/consulate
10	**<u>For Toll Companies</u>** Last Valid Updated Toll Card /Annex including the requested Manufacturing/ Packaging site

5.27.3. Replacement or addition of a Manufacturing/Packaging/Batch Releasing Site (Imported/UL / Bulk Products)	
1	**Fees:** 1st site change: 3000 L.E 2nd site addition/change: 5000 L.E 3rd site addition/change: 10000 L.E 4th site addition/change: 20000 L.E
2	**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 ****in case of the variation doesn't Mentioned in the CPP of the product (For Packaging/Batch Releasing Site)**
3	**Certificate of Good Manufacturing Practice (GMP)** For new site Valid Authenticated from Chamber of commerce & Egyptian consulate/embassy or Notary
4	**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 Authenticated by the Chamber of commerce or Notary & Egyptian consulate/embassy

5.27.4. Replacement or addition of a Storage Site	
1	**Fees:**1000 L.E
2	**Storage site License**
3	**<u>For Local FPP</u>**

	Storage contract: Between LH & Storage site. Valid. Authenticated from Bank & EDA Legal Affairs
4	**<u>For imported FPP</u>** ***Importer Rigester License (**stating the name of storage site**)** ***Declaration Letter** from license holder stating the importer of the product **(if required)**
5	**<u>For Bulk/UL FPP</u>** **storage contract** Between LH/Applicant & Storage Site Valid. Authenticated from Bank & EDA Legal Affairs. ***<u>If the contract is between the applicant & Storage site:</u>** A letter from LH/MAH authorizing the applicant to sign contracts Authenticated from chamber of commerce or Notary& Egyptian embassy/consulate
6	**<u>For Toll Companies</u>** Last Valid Updated Toll Card/Annex including the requested Storage site

5.28. Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product	
1	**Fees:** 1000 L.E.

2	Comparison between current & proposed Process on the Manufacturer Letter Head (Signed &Stamped)
3	**<u>For Local & UL Products</u>** **<u>EDA Inspection Report</u>** Stating the Following: *Currently approved manufacturing process & Mentioning the proposed manufacturing process of the finished product (With attached Flow Chart of The Current/Proposed Manufacturing Process) *Clarifying if this change will be accompanied by changes in qualitative and quantitative impurity profile or in physico-chemical properties Signed & stamped from EDA inspector **<u>UL/ Imported Products:</u>** Letter of Variation From License Holder stating the Change Authenticated from Chamber of Commerce , Egyptian Consulate /Embassy
4	**Declaration Letter** That the changes to process parameter(s) have no impact on the quality of the finished product.

5.29. Change in the batch size of the finished product	
Scaling up or down of FPP production batch size (Local/ UL / Imported Products)	
1	**Fees:** 1000 L.E.
2	**<u>For Local & UL Products</u>** **EDA** Inspection Report

	Stating the batch size of the 1st production batch in addition to the currently approved batch size & Mentioning the proposed batch size Clarifying if this change will be accompanied by changes in the manufacturing process or equipment Signed & stamped from EDA inspector
3	**<u>For UL & Imported Products</u>** **Letter of Variation** From Product LH in COO Stating the required variation
4	**Declaration Letter** Stating that "This change is for marketing reasons only with NO change in quality, manufacture and stability of the product"
5	**Declaration Letter** Stating that "The company didn't get a previous approval for batch size change for this product" In case presence of a previous approval, state number and date of the approval and attach it with the file
6	**Declaration Letter** Stating that "There is YES/No change in the manufacturing process" **In Case of YES Comparison between Old & New manufacturing process.
7	**Declaration Letter** Stating that "There is YES/No change in the manufacturing equipment except only those necessitated by the change in batch size (e.g. use of different sized equipment with same design & operating principle) **In Case of YES

	Declaration Letter stating the comparison between the Old & New manufacturing equipment.
8	**If New Registration license is registered according to 425 or 645 (in case of Change/Addition of Batch Size)** (Please clarify if change is related to the first three production batches manufactured **or /No**)

5.30. Change to in-process tests or limits applied during the manufacture of the finished product	
1	**Fees:** 1000 L.E.
2	Comparative table of current and proposed in-process control and limits.
3	Details of any new analytical procedure and validation data, where relevant
4	Justification/risk assessment showing that the in-process control is non-significant or that it is obsolete.
5	Justification of the new in-process control and limits.
6	Comparative study results or comparative analysis results showing that the current analytical procedure and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new analytical procedure.
7	All updated relevant sections of the CTD part related to the new change.

5.31. Change in the specification attribute and/or acceptance criteria of an excipient	
1	**Fees:** 1000 L.E.
2	Comparative table of current and proposed specifications.
3	Details of any new analytical procedure and validation data, where relevant.

4	Batch analysis data on two production batches of the excipient for all specification attributes [3 production batches (unless otherwise justified) for biological excipients or novel excipients].
5	Justification for not submitting a new bioequivalence study according to the relevant Guideline on The Investigation of Bioequivalence, if appropriate.
6	Justification/risk assessment showing that the attribute is non-significant or that it is obsolete.
7	Justification of the new specification attribute and the acceptance criteria.
8	All updated relevant sections of the CTD part related to the new change.

5.32. Change in the specification attribute and/or limits of the Finished Pharmaceutical product	
1	**Fees:** 1000 L.E.
2	Old Finished Pharmaceutical product specifications "signed and stamped".
3	New Finished Pharmaceutical product specifications "signed and stamped".
4	Comparative table of current and proposed specifications.
5	Scientific justification & Reference for the requested change
6	Pharmacopeia Monograph
7	All updated relevant sections of the CTD part related to the new change.

5.33. Change in test (Analytical) procedure for the Finished Pharmaceutical product	
1	**Fees:** 1000 L.E.
2	**Notification** /Approved CoA from CADC with proposed change
3	All updated relevant sections of the CTD part related to the new change.

5.34. Change in immediate packaging of the finished product	
1	**Fees:** 1000 L.E.
2	COAs of Old Packs containing full detailed description for type of pack, its capacity and liner.
3	COAs of New Packs from suppliers containing full detailed description for type of pack, its capacity and liner.
4	Comparative table of the current and proposed immediate packaging specifications, if applicable.
5	Sample.
6	In case of presence of desiccant, attach COA of desiccant supplier.
7	All updated relevant sections of the CTD part related to the new change.

5.35. Change in the specification attribute and/or acceptance criteria of the immediate packaging of the finished product	
1	**Fees:** 1000 L.E.
2	Comparative table of current and proposed specifications.
3	Details of any new analytical procedure and validation data, where relevant.
4	Justification/risk assessment showing that the parameter is non-significant or that it is obsolete.
5	Justification of the new specification attribute and the acceptance criteria.
6	All updated relevant sections of the CTD part related to the new change.

5.36. Change in analytical procedure for the immediate packaging of the finished product	
1	**Fees:** 1000 L.E.
2	Comparative table of current and proposed analytical procedure, if applicable.

3	Comparative validation results or if justified comparative analysis results showing that the current analytical procedure and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new analytical procedure.
4	Description of the analytical methodology, a summary of validation data.
5	All updated relevant sections of the CTD part related to the new change.

5.37. Change in shape of the container	
1	**Fees:** 1000 L.E.
2	COAs of Old Packs containing full detailed description for type of pack, its capacity and liner.
3	COAs of New Packs from suppliers containing full detailed description for type of pack, its capacity and liner.
4	Sample.
5	Reference for new shape.
6	All updated relevant sections of the CTD part related to the new change.

5.38. Change in pack size of the finished product	
1	**Fees:** 1000 L.E.
2	COAs of Old Packs containing full detailed description for type of pack, its capacity and liner.
3	COAs of New Packs from suppliers containing full detailed description for type of pack, its capacity and liner.
4	Sample.
5	Reference for new pack size.

6	All updated relevant sections of the CTD part related to the new change.

5.39. Change in any part of the primary packaging not in direct contact with the finished product formulation	
1	**Fees:** 1000 L.E.
2	COAs of Old Packs containing full detailed description for type of pack, its capacity and liner.
3	COAs of New Packs from suppliers containing full detailed description for type of pack, its capacity and liner.
4	Sample.
5	Reference for new pack (Related to change / addition accessory).
6	All updated relevant sections of the CTD part related to the new change.

5.40. Change in manufacturer, sterilization process or supplier of packaging components (when mentioned in the dossier).	
1	**Fees:** 1000 L.E.
2	Comparative table of current and proposed specifications, if applicable.
3	Description of the sterilization method and sterilization cycle. Validation of the sterilization cycle should be provided if the sterilization cycle does not use the reference conditions stated in the Ph. Eur.
4	Evidence that the sterilization has been conducted and validated in accordance with GMP and/or relevant ISO standards, as per guideline on the sterilization of the medicinal product, active substance, excipient and primary container.
5	All updated relevant sections of the CTD part related to the new change.

5.41. Change of a secondary packaging component of the finished product (including replacement or addition or deletion), when mentioned in the dossier	
1	**Fees:** 1000 L.E.
2	All updated relevant sections of the CTD part related to the new change.

5.42. Change in the shelf-life or storage conditions of the Finished Pharmaceutical product	
a. Reduction of the shelf life	
1	**Fees:** 1000 L.E.
2	Reference of Innovator
3	Scientific Justification for this Reduction.
4	Any Stability studies or documents for new shelf life that clarifying the need of reduction of shelf life must be submitted
5	**In Case of Imported or Under license Files:** Declaration Letter from LH/MAH in COO signed and stamped: Stating reasons of reduction.
6	All updated relevant sections of the CTD part related to the new change.
b. Extension of the shelf life	
1	**Fees:** 1000 L.E.
2	Stability study approval
3	All updated relevant sections of the CTD part related to the new change.
c. Change in storage conditions of the Finished Pharmaceutical product or the diluted/reconstituted product	
1	**Fees:** 1000 L.E.
2	Stability study approval

3	All updated relevant sections of the CTD part related to the new change.

IV) Additional human pharmaceutical variations Not reportable in Sixth edition guidelines:

5.43. Change Reg. Type of Finished product	
5.43.1. Change Reg. Type from Imported Finished to Imported Bulk	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**Letter of Variation** From LH/MAH Stating the transfer of Packaging site 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 or Notary & Egyptian consulate/embassy
3	**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 or Notary& Egyptian embassy/consulate is needed in case that the LH/MAH signing the contract.
4	**Attached Annex of the contract**

	The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
5	**Last Updated Packaging site license** Area needed for packaging the product is present
6	**Last Updated Commercial Register** Of the new packaging site
7	**Storage contract** Between LH/Applicant & Storage site. Valid. Authenticated from Bank & EDA Legal Affairs. Authentication form chamber of commerce or Notary& Egyptian embassy/consulate is needed in case that the LH/MAH signing the contract.
8	**Storage Site License**

5.43.2. Change Reg. Type from Imported Finished to UL	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**Letter of Variation** From LH/MAH Stating the transfer of Bulk Manufacturing Site 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 or Notary & Egyptian consulate/embassy

3	**Manufacturing Contract:** Between LH/Applicant & New manufacturer. A letter from LH/MAH authorizing the applicant to sign contracts Authenticated from Bank & EDA Legal Affairs. Authentication form chamber of commerce or Notary& Egyptian embassy/consulate is needed in case that the LH/MAH signing the contract.
4	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
5	**Last Updated Manufacturing site license:** Production line &/or area needed for manufacturing the product is present.
6	**Last Updated Commercial Register** (New Manufacturer)
7	**Storage contract** Between LH/Applicant & Storage site. Valid. Authenticated from Bank & EDA Legal Affairs. Authentication form chamber of commerce or Notary& Egyptian embassy/consulate is needed in case that the LH/MAH signing the contract.
8	**Submission of API supplier addition request.** Refer to API supplier addition checklist

5.43.3. Change Reg. Type from Imported Finished to Local	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**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 Chamber of commerce or Notary & Egyptian consulate/embassy
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	**Last Updated Manufacturing site license** Production line &/or area needed for manufacturing the product is present.
6	**Last Updated Commercial Register** (New Manufacturer)
7	**Storage contract:** Between New LH & Storage site. Valid.

	Authenticated from Bank & EDA Legal Affairs.
8	**Storage Site License**
9	**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
10	**Submission of API supplier addition request.** Refer to API supplier addition checklist

5.43.4. Change Reg. Type from UL to Imported Finished	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**Letter of Variation** From LH/MAH Stating the transfer of Bulk MFG Site 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 or Notary & Egyptian consulate/embassy
3	**Certificate of Good Manufacturing Practice (GMP)** For New Manufacturing site Valid & Authenticated from Chamber of Commerce or Notary & Egyptian Consulate/Embassy
4	**Manufacturing Waiver**

	From old manufacturer The product trade name & reg. no. is mentioned Authenticated from Bank & EDA Legal Affairs
5	**Last Updated Importer Record (stating name of storage site and product name)**

5.43.5. Change Reg. Type from UL to Imported Bulk	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**Letter of Variation** From LH/MAH Stating the transfer of Bulk Manufacturing Site 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 or Notary & Egyptian consulate/embassy
3	**Certificate of Good Manufacturing Practice (GMP)** For new Manufacturing site Valid Authenticated from Chamber of Commerce or Notary & Egyptian Consulate/Embassy
4	**Manufacturing Waiver** From old manufacturer The product trade name & reg. no. is mentioned Authenticated from Bank & EDA Legal Affairs

5	**Packaging contract (<u>In Case of Changing Packaging Site</u>)** 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 or Notary& Egyptian embassy/consulate is needed in case that the LH/MAH signing the contract.
6	**Last Updated Importer Record**

5.43.6. Change Reg. Type from UL to Local	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**Letter of Variation** From LH/MAH Stating the transfer of ownership of the product with clarification of the consequential changes and <u>justification</u> for this change The product trade name & reg. no. is mentioned Authenticated by the Chamber of commerce or Notary & Egyptian consulate/embassy
3	**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
4	**In case of Toll Manufacturing:**

	Manufacturing contract: Between LH & New manufacturer/packager. Authenticated from Bank & EDA Legal Affairs.
5	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
6	**Last Updated Manufacturing site license** Production line &/or area needed for manufacturing the product is present.
7	**Storage contract:** Between LH/Applicant & Storage site. Valid. Authenticated from Bank & EDA Legal Affairs.
8	**Storage Site License**
9	**3 Copies Composition declaration:** On New LH Letterhead Signed & stamped Identical to the one attached with the registration license or to the latest finally approved composition

5.43.7. Change Reg. Type from Imported Bulk to Imported Finished	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)

2	**Letter of Variation** From LH/MAH Stating the transfer of Packaging site 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 or Notary & Egyptian consulate/embassy
3	**Waiver** From old packager The product trade name & reg. no. is mentioned Authenticated from Bank & EDA Legal Affairs
4	**Certificate of Good Manufacturing Practice (GMP)** For new packaging site Valid Authenticated from Chamber of Commerce & Egyptian Consulate/Embassy

5.43.8. Change Reg. Type from Imported Bulk to UL	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**Letter of Variation** From LH/MAH Stating the transfer of Bulk MFG site 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 or Notary & Egyptian consulate/embassy
3	**In case of Toll Manufacturing:** **Manufacturing contract** Between LH/Applicant & New Manufacturer. Valid. 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.
4	**Attached Annex of the contract** The product trade name & reg. no. is mentioned. Authenticated from Bank & EDA Legal Affairs
5	**Last Updated Manufacturing site license** Production line &/or area needed for manufacturing the product is present.
6	**Last Updated Commercial Register** (New Manufacturer)
7	**Packaging Waiver** From old packager (In case of changing packaging site) The product trade name & reg. no. is mentioned Authenticated from Bank & EDA Legal Affairs
8	**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.
9	**Storage Site License**
10	**Submission of API supplier addition request.** Refer to API supplier addition checklist

5.43.9. Change Reg. Type from Imported Bulk to Local	
1	**Fees:** 1000 L.E (In addition to additional fees concerning consequential variations)
2	**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
3	**In case of Toll Manufacturing:** **Manufacturing contract** Between New LH & New Manufacturer. 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	**Latest Updated Manufacturing site license** Production line &/or area needed for manufacturing the product is present.
6	**Last Updated Commercial Register** Of the new manufacturing site
7	**Packaging Waiver <u>(In case of Changing Packaging Site)</u>** From old packager The product trade name & reg. no. is mentioned Authenticated from Bank & EDA Legal Affairs
8	**Storage contract** Between New LH & 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.
9	**Storage Site License**
10	**3 Copies of Composition declaration** On New LH Letterhead

	Signed & stamped Identical to the one attached with the registration license or to the latest finally approved composition
11	**Submission of API supplier addition request.** Refer to API supplier addition checklist

5.44 Updating Analysis File	
1	**Fees:** 1000 L.E.
2	* **150 EDA Chairman Renewal Approval** * CADC Labs Analysis Certificate **OR** A "Not Found" Letter from CADC

5.45. Clarification / Change of salt equivalence and/or crystalline state (e.g. hydrate, solvate, polymorph)	
1	**Fees:** 1000 L.E.
2	Old composition "signed and stamped".
3	New composition "signed and stamped".
4	Comparison table between old and new composition.
5	Scientific Reference for Molecular weight of base and salt. (e.g. Pharmacopeia).
6	Calculations of salt equivalence on applicant paper signed and stamped.
7	Innovator Reference stating the salt form and its quantity.
8	C.O.A & Composition of all suppliers of Active Ingredient or Premixes.

9	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.
10	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.
11	All updated relevant sections of the CTD part related to the new change.

5.46. Clarification /Change of particle size for water Insoluble or sparingly soluble API (Particle size must be stated in suppliers COA by D90 or mesh size)	
1	**Fees:** 1000 L.E.
2	Old composition "signed and stamped"
3	New composition "signed and stamped"
4	Comparison table between old and new composition
5	C.O.A of all suppliers for active ingredient stated D 90 or mesh size
6	Stating Range of D90 in New Composition.
7	A report from Inspection Department stating the Range of D90 of used materials (In case of Clarifying Particle Size).
8	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).
9	All updated relevant sections of the CTD part related to the new change.

5.47. Clarification /Change or Addition of the solvents used in manufacturing process (e.g. ethanol, methanol)

1	**Fees:** 1000 L.E.
2	Old composition "signed and stamped"
3	New composition "signed and stamped"
4	Comparison table between old and new composition
5	Declaration Letter States class of the solvent according to USP Classification.
6	In New Composition; write the solvent used & that it is totally evaporated during manufacturing process.
7	In case of Clarification: inspection report including Batch Record for old production batches clarifying that the solvent was used before
8	Inspection analysis including residual solvent test (in case of clarification)
9	All updated relevant sections of the CTD part related to the new change.

5.48. Clarification /Change of Active / Inactive Ingredient Specification:	
1	**Fees:** 1000 L.E.
2	Pharmacopeia Monograph (Last Edition)
3	C.O.A of all suppliers of Active Ingredient or Premixes.
4	Comparison between Old & New Finished Pharmaceutical Product Specification signed and stamped.
5	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 or in case of suppliers are not stated in registration license)
6	Old composition "signed and stamped"
7	New composition "signed and stamped"
8	Comparison table between old and new composition.

9	All updated relevant sections of the CTD part related to the new change.

5.49. Change in Color of Finished Pharmaceutical product	
1	**Fees:** 1000 L.E.
2	Sample (IF Needed).
3	Old & New Certificate of Analysis.
4	Pharmacopeia Monograph & Certificate of analysis of supplier of active ingredient or pellets or premixes (In Case of Change in Range of color without any qualitative or quantitative change in composition).
5	Scientific Justification for color change with scientific reference.
6	Manufacturing process flow chart (In case of the Change in physical character is due to change in Manufacturing process).
7	Composition of capsule shell on supplier paper (In case of Change color of capsule shell).
8	All updated relevant sections of the CTD part related to the new change.

5.50. Correcting Dosage Form	
1	**Fees:** 1000 L.E.
2	Innovator reference and it's leaflet.
3	Any studies issued previously for New Dosage form.
4	All updated relevant sections of the CTD part related to the new change.

5.51. Change / Addition of Route of Administration	
1	**Fees:** 1000 L.E.

2	Reference for Innovator and its leaflet.
3	Any Studies issued previously for New Route of Administration.
4	In case of Infusion: Submit declaration, letter stating the used solvent for infusion.
5	All updated relevant sections of the CTD part related to the new change.

5.52. Change in supplier of packaging components / devices	
1	**Fees:** 1000 L.E.
2	COAs of Old Packs containing full detailed description for type of pack, its capacity and liner.
3	COAs of New Packs from suppliers containing full detailed description for type of pack, its capacity and liner.
4	Sample.
5	Certificate of device.
6	All updated relevant sections of the CTD part related to the new change.
7	A copy of the Inspection sampling report, stating the batch number and the date of its production
8	In case of physical description of the product differs from CADAC description, submit request for clarifying physical character to comply with CADAC Final report.

5.53. Change in secondary packaging component of the active Substance	
1	**Fees:** 1000 L.E.
2	Amendment of the relevant section(s) of the dossier.
3	All updated relevant sections of the CTD part related to the new change.

V) Documents for Reliance Evaluation Route:

In addition to common Administrative &Relevant documents the following documents should be submitted for Good Practice of Reliance Post Approval variations

Fees: 1000 L.E. **Fees for Registration batch analysis:** 15.000 L.E. (For one batch) **Fees for Inspection batch analysis:** 3.000 L.E. (For one batch) **Fees for Competitive study:** 2000 L.E.(For one batch)	
In Case of Finished pharmaceutical product imported from non-reference country and not marketed in a reference country	
1	The approval of another NRA
2	Sameness Letter
3	The studies conducted in country of origin
In Case of Imported Finished product that has been approved Variation Requests by at least one reference regulatory authority (SRA) or WHO prequalification.	
1	Sameness letter.
2	Unredacted Assessment report (otherwise justified with evidence).
3	Application submitted to the SRA.
4	Proof of approval from at least one reference regulatory authority (otherwise justified with evidence).
5	A linking between the application and the approval from the Reference Authority (unless otherwise justified).
6	A linking between the application and supportive documents (unless otherwise justified).
7	Approval issued by the SRA.
8	Updated sections of the CTD.

- **The Applicants can submit Post-Approval Changes (PACs) that may not state in EDA Guidelines. However, EDA will evaluate the change through a risk-based assessment to ensure compliance with safety, efficacy, and quality standards. If a PAC is found to be non-compliant to the EDA regulations and guidelines. EDA may require additional information or reject the request.**
- **The non-sequential order of versions of the Common Technical Document (CTD) makes the reliance evaluation unreliable as the company must submit the updated version contains all sequential updates.**
- **EDA relies on Approval issued by the SRA of the entire group of variations as a grouping variation; therefore, the applicant must submit all variations mentioned in this approval.**

- **In case of submission Human Pharmaceutical Post Marketing Variation Approval request, It must be submitted according to structured CTD format as follow:**

3.1 Table of Contents of Module
3.2 Body of Data
3.2.S DRUG SUBSTANCE
3.2.S.1 General Information
3.2.S.1.1 Nomenclature
3.2.S.1.2 Structure
3.2.S.1.3 General Properties
3.2.S.2 Manufacture
3.2.S.2.1 Manufacturer(s)
3.2.S.2.2 Description of Manufacturing Process and Process Controls
3.2.S.2.3 Control of materials
3.2.S.2.4 Controls of critical steps and intermediates
3.2.S.2.5 Process validation and/or evaluation
3.2.S.2.6 Manufacturing process development
3.2.S.3 Characterization

3.2.S.3.1 Elucidation of structure and other characteristics
3.2.S.3.2 Impurities
3.2.S.4 Control of the API
3.2.S.4.1 Specification
3.2.S.4.2 Analytical procedures
3.2.S.4.3 Validation of analytical procedures
3.2.S.4.4 Batch analyses
3.2.S.4.5 Justification of specification
3.2.S.5 Reference standards or materials
3.2.S.6 Container-closure system
3.2.S.7 Stability
3.2.S.7.1 Stability summary and conclusions
3.2.S.7.2 post-approval stability protocol and stability commitment

3.2.P DRUG PRODUCT (OR FINISHED PHARMACEUTICAL PRODUCT (FPP))
3.2.P.1 Description and composition of the FPP
3.2.P.2 Pharmaceutical Development
3.2.P.2.1 Components of the FPP
3.2.P.2.1.1 Active pharmaceutical ingredient
3.2.P.2.1.2 Excipients
3.2.P.2.2 Finished pharmaceutical
product 3.2.P.2.2.1 Formulation
development 3.2.P.2.2.2 Overages
3.2.P.2.2.3 Physicochemical and biological properties
3.2.P.2.3 Manufacturing process development
3.2.P.2.4 Container-closure system
3.2.P.2.5 Microbiological attributes
3.2.P.2.6 Compatibility
3.2.P.3 Manufacture
3.2.P.3.1 Manufacturer(s)
3.2.P.3.2 Batch formula

3.2.P.3.3 Description of manufacturing process and process controls
3.2.P.3.4 Controls of critical steps and intermediates
3.2.P.3.5 Process validation and/or evaluation
3.2.P.4 Control of excipients
3.2.P.4.1 Specifications
3.2.P.4.2 Analytical procedures
3.2.P.4.3 Validation of analytical procedures
3.2.P.4.4 Justification of specifications
3.2.P.4.5 Excipients of human or animal origin
3.2.P.4.6 Novel excipients
3.2.P.4 Control of FPP
3.2.P.5.1 Specifications
3.2.P.5.2 Analytical procedures
3.2.P.5.3 Validation of analytical procedures
3.2.P.5.4 Batch analyses
3.2.P.5.5 Characterization of impurities
3.2.P.5.6 Justification of specification(s)
3.2.P.6 Reference standards or materials
3.2.P.7 Container-closure system
3.2.P.8 Stability
3.2.P.8.1 Stability summary and conclusions
3.2.P.8.2 post-approval stability protocol and stability commitment
3.2.P.8.3 Stability data
3.2.A APPENDICES
3.2.A.1 Facilities and Equipment
3.2.A.2 Adventitious Agents Safety Evaluation
3.2.A.3 Excipients
3.2.R.1 Production documentation
3.2.R.1.1 Executed production documents
3.2.R.1.2 Master production documents
3.2.R.2 Analytical procedures and validation information
3.3 Literature References

Variation Application Form of Post Marketed Human Products

***Notes: -Annex I&II shall be fulfilled**

-Annex III fulfilled according to the submitted variation

Annex I: Product Information , Classification of Proposed Changes and General Amendments and Data	
1-Product Information	
Trade Name:	**Applicant:**
Dosage form:	**License Holder/MAH :**
Active substance(s):	**Manufacturer of Finished Pharmaceutical product:**
Concentration:	**Primary /Secondary Packager/Batch Releaser:**
Registration Decree:	**Manufacturer of solvent:**
Registration number:	**Storage Site:**
Type of License:	**Type of Marketing:**
2-Classification of the Submitted Variation According to Variation Guidelines	
-Mode of Submission: (Tick √) ○ **Single PAC** ○ **Grouped PAC**	
-Variation Evaluation Route: (Tick √) ○ **Full Evaluation Route** ○ **Reliance Evaluation Route**	
-Categorization of submission: (Tick √) ○ **Appeal** ○ **Inquiry with assessment** ○ **Inquiry without assessment** ○ **Post Marketing Variation approval** ○ **Reliance route**	
-Type of the request: (Tick √) ○ **Administrative Change**	

- **Quality Change**

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			
Imprints / Embossing / other marking			
Scoring			
Shape of pharmaceutical finished product			
Dimensions of pharmaceutical finished product			
Excipient			
Coating weight / weight of capsule shell			
Color of (coat / capsule shell, etc ….)			
Specification of Finished Pharmaceutical product			
Shelf life			
	Change	**Addition**	**Clarify**
Storage Conditions			
API form as salt equivalence and/or crystalline state			
Test procedure			
The particle size of API (state D90)			
Solvents			
Specification of Active ingredient			
Specification of Inactive ingredients			
Route of Administration			
Dosage Form			
B) Container Closure System Changes As:			
Primary packaging of finished pharmaceutical product			
Shape of container			
Pack size of finished pharmaceutical product			
Part of primary packaging material not in contact with the finished product formulation			
Supplier of packaging components / Devices			
Clarify the change concerning which type of packs: Local/Tender/Export/Hospital use			
C) Ownership / Manufacturing Changes As:			
Name of License holder			
Address of License holder			
Name of Manufacturer site (Bulk manufacture or Packager or Batch releaser)			

Address of Manufacturer site			
Applicant for Registration			
Modification of Registration License			
License Holder /MAH Transfer			
Marketing Rights holder			
Marketing Authorization holder in **Egypt**			
Solvent Manufacturer			
Manufacture site			
Primary Packager			
Secondary Packager			
Batch Releaser			
Storage Site			
Batch size factor of 10 X			
Batch size over 10 X			
Change Registration Type			
Addition of Manufacturer for Export only			
In-Process Control			
Manufacturing process			
	Change	**Addition**	**Clarify**
D) API Manufacturer changes as:			
Name of API Manufacturer			
Address of API Manufacturer			
Deletion of API Manufacturer			
API Manufacturer (with DMF or Not)			
Manufacturing process of API			
Batch size of API			
In process tests during the manufacture of API			
Specification parameters &/or limits of API			
Test Procedures during the manufacture of API			
Primary packaging of API			
Retest period/storage period of API			
Storage condition of API			
CEP			
E) Miscellaneous			**Tick for required Issue**
Extensions			
Updating Analysis File			
Cancelling previous variation approvals			
Re-issuing Approvals			
Non-Reportable Requests:			

(Please Describe the request)		
3-kindly fulfill the following Amendments by Yes / NO	**Yes**	**No**
1- Is All documents & information submitted in the file are correct and on the responsibility of the applicant		
2- Is the submitted file contains all the approvals for the product that were not mentioned in the last released registration license		
3- Is the submitted file contains the latest issued registration license		
4- Is the submitted file contains Valid registration license **(In case of Invalidation Please submit registration renewal or validity extension)**		
5- Is the submitted file contains Valid Pricing license		
6- Is the submitted EDA lab composition and its certificate of analysis is the last composition analyzed by CADC Labs.		
7- Is the submitted file contains all approvals, variations, decisions & exemptions issued for the product from different EDA departments		
8- Is the submitted request fulfilling all conditions stated in guidelines		
9- Is the Approved Manufacturing Site (s)Capable for secondary packaging of the product (In case of change /addition of pack or In case of Change /Addition of Manufacturing Site)?		
4-Kindly state the following data:		
1- In case of Any previous variations' approvals, variations, decisions & exemptions issued for the product from different 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: Is a Ministerial decree 600/2018 exemption approval **(If needed)** is Attached: **Yes / No**		
3- If New Registration license is registered according to 425 or 645 **(In case of Batch Size)** (Please clarify if change is related to first three production batches manufactured or No) **Yes / No**		
4- Status from submission to pharmacovigilance (In case of changing the applicant)		

5- 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, Type of variation.
6- Name & address of Manufacturers of API of product as stated in GMP Name & address of suppliers of API of product
7- Please Clarify the Following A- BCs Class of Active Substance: (Kindly attach Biopharmaceutics Classification System **Reference**) ☐ Class I ☐ Class II ☐ Class III ☐ Class IV B- The Product Is Innovator: ☐ Yes ☐ No

Annex II Technical Justification & Supportive Data

1- Summary of Change (Please give detailed explanation for the proposed changes)	
Current Approved Status	**Proposed Status**
2-Scientific Justification & Reason for Change (In detailed description for the reason of change)	
3-Impacted CTD Parts (s): (According to the CTD relevant parts) Tick (√)on the relevant module	
○ Module 1 (Administrive /Labeling)	○ Module 3 (Quality /CMC)
4-Impacted CTD Parts (s): (According to the CTD relevant parts) Tick (√)on the relevant part	
Module 3	
○ 3.1 Table of Contents of Module ○ 3.2 Body of Data ○ 3.2.S DRUG SUBSTANCE	○ 3.2.P.2.2.1 Formulation development ○ 3.2.P.2.2.2 Overages ○ 3.2.P.2.2.3 Physicochemical and biological properties

- 3.2.S.1 General Information
- 3.2.S.1.1 Nomenclature
- 3.2.S.1.2 Structure
- 3.2.S.1.3 General Properties
- 3.2.S.2 Manufacture
- 3.2.S.2.1 Manufacturer(s)
- 3.2.S.2.2 Description of Manufacturing Process and Process Controls
- 3.2.S.2.3 Control of materials
- 3.2.S.2.4 Controls of critical steps and intermediates
- 3.2.S.2.5 Process validation and/or evaluation
- 3.2.S.2.6 Manufacturing process development
- 3.2.S.3 Characterization
- 3.2.S.3.1 Elucidation of structure and other characteristics
- 3.2.S.3.2 Impurities
- 3.2.S.4 Control of the API
- 3.2.S.4.1 Specification
- 3.2.S.4.2 Analytical procedures
- 3.2.S.4.3 Validation of analytical procedures
- 3.2.S.4.4 Batch analysis
- 3.2.S.4.5 Justification of specification
- 3.2.S.5 Reference standards or materials
- 3.2.S.6 Container-closure system
- 3.2.S.7 Stability
- 3.2.S.7.1 Stability summary and conclusions
- 3.2.S.7.2 post-approval stability protocol and stability commitment
- 3.2.P DRUG PRODUCT (OR FINISHED PHARMACEUTICAL PRODUCT (FPP))
- 3.2.P.1 Description and composition of the FPP
- 3.2.P.2.3 Manufacturing process development
- 3.2.P.2.4 Container-closure system
- 3.2.P.2.5 Microbiological attributes
- 3.2.P.2.6 Compatibility
- 3.2.P.3 Manufacture
- 3.2.P.3.1 Manufacturer(s)
- 3.2.P.3.2 Batch formula
- 3.2.P.3.3 Description of manufacturing process and process controls
- 3.2.P.3.4 Controls of critical steps and intermediates
- 3.2.P.3.5 Process validation and/or evaluation
- 3.2.P.4 Control of excipients
- 3.2.P.4.1 Specifications
- 3.2.P.4.2 Analytical procedures
- 3.2.P.4.3 Validation of analytical procedures
- 3.2.P.4.4 Justification of specifications
- 3.2.P.4.5 Excipients of human or animal origin
- 3.2.P.4.6 Novel excipients
- 3.2.P.4 Control of FPP
- 3.2.P.5.1 Specifications
- 3.2.P.5.2 Analytical procedures
- 3.2.P.5.3 Validation of analytical procedures
- 3.2.P.5.4 Batch analyses
- 3.2.P.5.5 Characterization of impurities
- 3.2.P.5.6 Justification of specification(s)
- 3.2.P.6 Reference standards or materials
- 3.2.P.7 Container-closure system
- 3.2.P.8 Stability
- 3.2.P.8.1 Stability summary and conclusions
- 3.2.P.8.2 post-approval stability protocol and stability commitment
- 3.2.P.8.3 Stability data

○ 3.2.P.2 Pharmaceutical Development ○ 3.2.P.2.1 Components of the FPP ○ 3.2.P.2.1.1 Active pharmaceutical ingredient ○ 3.2.P.2.1.2 Excipients ○ 3.2.P.2.2 Finished pharmaceutical product	○ 3.2.A APPENDICES ○ 3.2.A.1 Facilities and Equipment ○ 3.2.A.2 Adventitious Agents Safety Evaluation ○ 3.2.A.3 Excipient
Module 1 **(Write the parts will be affected)**	
5-Risk based-Assessment For the Change (If needed) **(If the Varition not reportable in the guidelines submit the risk based assessment for the required change)**	

Annex III Supportive documents for submissions

-Supportive Documents for Post Marketing Variation Approval & Inquiry with Assessment Submissions

1-Supportive documents for DMF

- Comparison between the specifications of current suppliers, and proposed suppliers according to the monograph, as follows:

Items	Specifications according to the monograph	Current Suppliers COA Specification Limits	Specification (S4.1) of Current Suppliers in case it is supported by DMF	Proposed Suppliers COA Specification Limits	Specification (S4.1) of Proposed Suppliers	Justification for any differences (if needed)

- Submit the following DMF sections as **a PDF (in a separated folder)**
  - Manufacturer S.2.1
  - Organic impurities & residual solvents (S.3.2)
  - Specifications of API S.4.1
  - Batch analysis S.4.4
  - Container closure system S.6
  - Stability Specification S.7.1 & S.7.2
  - GMP with License
  - Letter of Access and Statement of Commitment

N.B.

Comparison should be made for specification values, not the result value

2-In Case of Change of API Specification and Finished product Specification submitted for Inquiry with assessment			
-In case of Finished product specification			
Items	**Old Finished product Specifications**	**New Finished product Specifications**	**Justification for any differences (If Needed)**

Note: Mention all tests, please specify the applicable reference or standard, indicating whether the test is based on an in-house method or a pharmacopeial reference.

-In Case of API Specification			
Items	**Specification limit of COA of old supplier(s)**	**Specification limit of COA of old supplier(s)**	**Tests mentioned in monograph**

Note: Mention all tests, please specify the applicable reference or standard, indicating whether the test is based on an in-house method or a pharmacopeial reference.

-In Case of any differences please Justify :

3- In Case of Submission of a Post-Marketing Variation Approval:
- Submit Required Supporting Studies & Comparison

***The submission shall include the following documents:**	**Yes**	**No**	**No. of Batches**
1-Batch Analysis Data: [No.of batches - Result:(e.g. Conform/Non-conform)]			
2-Stability Data: [type of study (6 months Accelerated & Long-term) ,Result: (e.g.. Pass) & Date of Approval.]			
3-Comparative dissolution study / bioequivalence. Result: conform.]			

4-Process Validation Report: [3 consecutive batches successfully produced – type of Batches (pilot or production)]			

***Comparison**

Items	Appoved Finished Product Specification 3.2.P.5.1	CADAC Specification	Stability Approval Specification	Stability data 3.2.P.8.3	Justification for any differences (If Needed)

Note: Mention all tests, please specify the applicable reference or standard, indicating whether the test is based on an in-house method or a pharmacopoeial reference.

-In Case of any differences please Justify :

For Inquiry without assessment Submission

Please Answer the following question:

	Yes	No
If the submitted request will affect the approved specifications of the finished product?		

***Note: Please Attach The cover letter mentioned in (Annex II Declarations template 5)**

For Appeal Submission

***Full Description of the appeal:**
***Applicant Justification**:
***Supportive Documents/Studies (Attach the approvals of the studies)**

For Reliance Evaluation Route Submissions

1. Administrative & Reference Authority Checklist

Please ensure the following mandatory documents are submitted in accordance with EDA Reliance Guidelines:

#Required Document / Requirement:

1-Valid Certificate of Pharmaceutical Product (CPP)

☐ Yes ☐ No

2- Updated Relevant Sections of CTD Dossier
Must include all sequential updates/versions to ensure evaluation reliability (However, the non-sequential order of versions of the Common Technical Document (CTD) makes the reliance evaluation unreliable as the company must submit the updated version contains all sequential updates)
☐ Yes ☐ No

3- Verification of Sameness (Sameness Letter)
Signed declaration confirming product identity with the reference product.
☐ Yes ☐ No

4- Unredacted Assessment Report and/or Q&A
Full report without redactions (unless officially justified).
☐ Yes ☐ No

5- Proof of Approval from Reference Authority
Official approval letter or certificate from at least one reference regulatory body.
☐Yes ☐ No

6- Reference Authority Application Copy
Clear linkage between the submitted application and the approval must be declared
☐ Yes ☐ No

2. Stability & Climatic Zone Declaration

- Approved Climatic Zone in Country of Origin:

☐ Zone II ☐ Zone IVa ☐Zone IVb ☐ Other (Specify: _____)

3. Type of Variation according to the Approval from Refernce Authority

Minor variations of Type IA ☐Yes ☐ No
Minor variations of Type IAIN ☐ Yes ☐ No
Minor variations of Type IB ☐ Yes ☐ No
Major variations of Type II ☐ Yes ☐ No

Where a group of variations consists of different types of variation, the group must be submitted and handled according to the 'highest' variation type included in the group.

4. Quality & Technical Supporting Data Checklist

No of Studies done According to the variation: _____

1- Batch Analysis Data

☐ Yes ☐ No

- No. of Batches: ----------
- Batches numbers: ----------
- Production & Expired date: ---------- _

- Attached Summary of Results (3.2.P.5.4 Batch analyses) ☐ Yes ☐ No
- Results: ☐ Conform ☐ Non-Conform

2 -Stability Data (6 Months Accelerated & Long-Term)

☐ Yes ☐ No

- No. of Batches: ----------
- Batches numbers: ----------
- Production & Expired date: ----------
- Type of stability study: ----------
- Attached Results (3.2.P.8 Stability/3.2.P.8.1 Stability summary and conclusions/3.2.P.8.2 post-approval stability protocol and stability commitment)

  ☐ Yes ☐No
- Results: ☐ Conform ☐ Non-Conform

3 -Comparative Dissolution Study / Bioequivalence

☐ Yes ☐ No

- No. of Batches: ----------
- Batches numbers: ----------
- Production & Expired date: ----------
- Type of study: ----------
- Results: ☐ Conform ☐ Non-Conform

4 -Process Validation Report

☐ Yes ☐ No

- Batch Type: ☐ Pilot ☐ Production
- Status: ☐ Successful (3 Consecutive)

Note: All non-sequential CTD submissions or incomplete assessment reports must be accompanied by an official scientific and regulatory justification letter signed by the License Holder.

5. Additional Supportive Documents

"The applicant must ensure that the Common Technical Document (CTD) for the product in Egypt is fully aligned with that of the reference country, accompanied by the corresponding CTD sections. This documentation acts as verification evidence to confirm that the product details provided in the Product Registration License remain unchanged." therefore It is mandatory submit the following sections:

☐3.2.P.1 Description and composition of the FPP

☐3.2.P.5.1 Specifications

☐3.2.P.7 Container-closure system

I hereby declare that all information and accompanying supporting data provided in this application and dossier are accurate, authentic, and complete. The proposed variation complies with all regulatory and quality standards.	
-Signature by the Authorized Person: **-Official Title:** **-Date:**	**-Company Stamp**

Annex II: Declarations

(In case of License holder Transfer -Addition of Manufacturing Site -Inquiry Without Assessment/Fullfilling Studies)

***Note: All declarations (of the request) shall be submitted attached with the application**

Template 1

السيد / رئيس الإدارة المركزية للمستحضرات الصيدلية

الإدارة العامة لتسجيل المستحضرات البشرية

إدارة المتغيرات للمستحضرات البشرية

تحية طيبة وبعد،،،،،

بخصوص المستحضر الآتي:

Trade Name:		
Dosage Form:		
Active Ingredients / Strength:		
Registration No.:		
Applicant Company:		
License Holder / MAH:		
Manufacturer / Packager:		
License Validity:	○ Valid ○ In-valid	Re-Reg 296/2009 Re-Reg 425/2015 Re-Reg 150/2022
Current status:		
Proposed status:		

أتعهد أنا ..... رئيس مجلس إدارة شركة .....(المالك القديم للمستحضر) ..... بأن المستحضر ليس له تركيزات أخرى من نفس الشكل الصيدلي أو أشكال صيدلية أخرى مسجلة أو تحت التسجيل مملوكة للشركة.

و تفضلوا بقبول وافر الإحترام والتقدير،،،،،

رئيس مجلس ادارة الشركة **ختم الشركة**

Template 2

السيد / رئيس الإدارة المركزية للمستحضرات الصيدلية

الإدارة العامة لتسجيل المستحضرات البشرية

إدارة المتغيرات للمستحضرات البشرية

تحية طيبة وبعد،،،،

بخصوص المستحضر الآتي:

Trade Name:		
Dosage Form:		
Active Ingredients / Strength:		
Registration No.:		
Applicant Company:		
License Holder / MAH:		
Manufacturer / Packager:		
License Validity:	○ Valid ○ In-valid	Re-Reg 296/2009 Re-Reg 425/2015 Re-Reg 150/2022
Current status:		
Proposed status:		

أتعهد أنا ..... رئيس مجلس إدارة شركة .....(المالك الجديد للمستحضر) ..... بأن المستحضر ليس له تركيزات أخرى من نفس الشكل الصيدلي أو أشكال صيدلية أخرى مسجلة أو تحت التسجيل مملوكة للشركة.

و تفضلوا بقبول وافر الإحترام والتقدير،،،،

رئيس مجلس ادارة الشركة **ختم الشركة**

Template 3

السيد / رئيس الإدارة المركزية للمستحضرات الصيدلية

الإدارة العامة لتسجيل المستحضرات البشرية

إدارة المتغيرات للمستحضرات البشرية

تحية طيبة وبعد،،،،،

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

Registered Product				Under-Registration Products			
	Trade Name / Dosage Form	API / Strength	Reg. Decree		Trade Name / Dosage Form	API / Strength	Reg. Decree

و تفضلوا بقبول وافر الإحترام والتقدير،،،،

رئيس مجلس ادارة الشركة **ختم الشركة**

Template 4

السيد / رئيس الإدارة المركزية للمستحضرات الصيدلية

الإدارة العامة لتسجيل المستحضرات البشرية

إدارة المتغيرات للمستحضرات البشرية

تحية طيبة وبعد،،،،

بخصوص المستحضر الآتي:

Trade Name:		
Dosage Form:		
Active Ingredients / Strength:		
Registration No.:		
Applicant Company:		
License Holder / MAH:		
Manufacturer / Packager:		
License Validity:	○ Valid ○ In-valid	Re-Reg 296/2009 Re-Reg 425/2015 Re-Reg 150/2022
Current status:		
Proposed status:		

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

وتفضلوا بقبول وافر الإحترام والتقدير،،،،

رئيس مجلس ادارة الشركة **ختم الشركة**

Template 5

الإدارة العامة لتسجيل المستحضرات البشرية

إدارة المتغيرات للمستحضرات البشرية

تحية طيبة وبعد،،،،،

بخصوص المستحضر الآتي:

Trade Name:		
Dosage Form:		
Active Ingredients / Strength:		
Registration No.:		
Applicant Company:		
License Holder / MAH:		
Manufacturer / Packager:		
License Validity:	○ Valid ○ In-valid	Re-Reg 296/2009 Re-Reg 425/2015 Re-Reg 150/2022

Current Status	Proposed Status	Justification for the change

***اتعهد انا شركة..... بان الطلب المقدم لادارة المتغيرات inquiry without assessment وبان التغيير المذكور اعلاه سوف (يؤثر /لا يؤثر) علي المواصفات النهائية للمستحضر وان الشركة سوف تقوم بالتغيير علي مسؤليتها**

و تفضلوا بقبول وافر الإحترام والتقدير،،،،،

رئيس مجلس ادارة الشركة **ختم الشركة**

Template 6

- Kindly submit comparison between the specifications of current suppliers, and proposed suppliers according to the monograph, as follows:

Specifications according to the monograph	Current Suppliers COA Specification Limits	Specification (S4.1) of Current Suppliers in case it is supported by DMF	Proposed Suppliers COA Specification Limits	Specification (S4.1) of Proposed Suppliers

- Kindly submit the following DMF sections as **a PDF (in a separated folder)**
  - Manufacturer S.2.1
  - Organic impurities & residual solvents (S.3.2)
  - Specifications of API S.4.1
  - Batch analysis S.4.4
  - Container closure system S.6
  - Stability Specification S.7.1 & S.7.2
  - GMP with License
  - Letter of Access and Statement of Commitment

N.B.

Comparison should be made for specification values, not the result values

Kindly fill in the attached application

رئيس مجلس ادارة الشركة **ختم الشركة**

Ensure all of the following sections are ticked in the table and uploaded

DMF section	Tick	Details
S1		Particle size in details (if available)
Physical appearance		
Solubility profile		
Melting point		polymorphism in details (if available)
pH		
Optical rotation		
Polymorphism		
S2.1		
S3		
XRPD only if the API has polymorphism		
elemental risk assessment		
genotoxic risk assessment		
nitrosamines risk assessment		
benzne risk assessment		
S4.1		check that microbiological and **sterility tests (if relevant)** are provided in both S4.1 and S4.4
S4.4		
S6		container closure system in details
S7.1		shelf life
S7.2		storage conditions
S7.3		

3 batches accelerated		
3 batches long term		

Document History:

Version No.	Issue Date	Summary of Change
1	06/01/2026	New Issue
2	15/10/2026	Update of Application Template