List of preclinical required documents in the file of the investigator and/or sponsor/CRO to be submitted to EDA for scientific opinion before First in human use

1. **Cover letter directed to Central Administration of Biological and Innovative products and clinical studies from applicant signed, dated and stamped clarifying the followings:**

   Applicant request, list of contents, aim of submission, type of investigational medicinal product, specification of the investigational medicinal product, proposed human use, dosage, strength and route of administration with overview of the nonclinical testing strategy

2. **Official Delegation letter stamped ,signed and dated from sponsor to the person who represent the company that will submit the documents to EDA.**

3. **Investigator's Brochure(IB):**

   Updated version of IB with its version and dateto document that relevant and current scientific information about the investigational product has been provided to the investigator. Compilation nonclinical data on the investigational product(s) that is relevant to the study of the product(s) in human subjects

4. **Signed agreement/ contract between involved parties,(To document agreements) e.g.:**
   - **Investigator/institution and sponsor**
   - **Investigator/institution and contract research organization (CRO)**
   - **Sponsor and contract research organization (CRO).**

5. **Curriculum vitae and/or other relevant documents evidencing qualifications of investigator(s) and/or supporting trial staff to whom investigator tasks are delegated**

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To document qualifications, GLP trainings and eligibility to conduct trial and/or provide medical supervision of subjects.

6. Certificate(s) of analysis of investigational product(s) e.g. identity, purity, and strength of investigational medicinal product(s) to be used in the trial.

7. Quality data ofinvestigational medicinal product;

To document the quality data of the IMP, cold chain reports ,stability study reports, batch release certificate from NRA of country of origin for the batch of the concerned investigational product ,...etc) .

8. The quality and safety of preclinical preparations should follow the strict control of the manufacturing process following the principles of good manufacturing practice (GMP).

9. Name of the laboratory, address, telephone number(s).

10. Evidence of accreditation and documented evidence of GLP compliance of the designated laboratories to be used for the assay of preclinicalsamples.

Certification or accreditation or established quality control and/or external quality assessment or other validation should be dated, signed and valid (where required).

11. Complete preclinical studies detailed reports for the investigational medicinal product are required to be submitted:

Preclinical data to be submitted

1) **Good Laboratory Practice (GLP) compliance of the studies: studies are expected to be performed in compliance with Good Laboratory Practice (GLP), However, there may be situations where full compliance with GLP is not possible. If the study, or part of the study, was not conducted in compliance with GLP, areas of noncompliance should be defined and a statement of the reason for noncompliance should be drawn up.**
2) **Specification of the test material: In general, the product that is used in the definitive pharmacology and toxicology studies should be comparable to the product proposed for the initial clinical studies. However, it is appreciated that during the course of**

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development programs, changes normally occur in the manufacturing process in order to improve product quality and yields. The potential impact of such changes for extrapolation of the animal findings to humans should be considered.

3) Reports on studies:

A. Pharmacology

- Primary and secondary pharmacodynamics studies of the product.
- Safety pharmacology studies.

B. Pharmacokinetics

- Pharmacokinetic studies of product.
- Specific Pharmacokinetic studies.
- Toxicokinetic.

C. Toxicology

- **Single-dose toxicity**
- **Repeat-dose toxicity**
- **Geno-toxicity (if applicable)**
- **Carcinogenicity *(Oncogenicity)* (if applicable)**
- **Immunotoxicity.**
- ***Immunogenicity.***
- **Local tolerance may be incorporated in toxicology studies).**
- **Reproductive & developmental toxicity (if applicable).**
- **Tissue Cross reactivity studies (if applicable).**
- **Environmental Risk Assessment.**

Note:

- **Specific guidelines should be followed for each type of product (biological, pharmaceutical, vaccine…etc) to be submitted.**
- **International Guidelines WHO-EMEA-FDA.**
- **Demonstration of relevance of the animal model; the relevance of the selected animal model should be justified in the application.**
- **Justification with documented evidence is required to be submitted in case of any item not fulfilled by the applicant.**

12. Signed and completed declarations by Investigators.

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13. Full, legible copies of key, peer-reviewed published articles supporting the application (when available).

14. Scientific advice opinion requirements from other regulatory authorities(if found).

15. Questions and answers between regulatory authorities and sponsor/applicant (if found).

16. Fees proof of payment:
Fees are 15,000 LE.

17. The Preclinical data should be submitted as two hardcopies and two soft copies (CD-ROM), and soft copy of data must be submitted electronically at ct@norcb.gov.eg.

18. Other supporting documents (if found).

Head of C.T.E. department **Head of CA of Biological andInnovative products and clinical studies**

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