## ضمیمه شماره ۴

## فرمت پیشنهادی پرونده اطلاعاتی برای ثبت

## ( Documentation For Registration)

**Part I:**
**IA: Administrative Data**
**IB: summary of product characteristics: ( product name – Therapeutic indications for the product – Pharmaceutical dosage form – Dosage and rout of administration – container ,closure and administration devices – packing sizes- shelf life)**
**, Labeling , Package Insert**
**IC: Expert reports**
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**Part II :Quality**
**IIA: Composition**
**1- Product Composition**

| Names of Substances | Quantity And /Or Percentage | Function/ Reason for inclusion | Refrence to Standard |
|---|---|---|---|
| Active Substane(s) | | | |
| Exipient(s) | | | |

2- Co**ntainer(Brief Description)**
**3- Clinical Trial Formula(E)**
**4- Development Pharmaceutics**

**IIB: Method of Preparation**
**1- Manufacturing Formula**
**(in cluding details of batch size)**
**2- Manufacturing Process**
**3- Validation of the Process**

**IIC: Control of Starting Material**
**1- Active Substanc(s)**
**1.1. specification and routin tests**
**1.1.1. Active substance(s) described in a pharmacopeia**
**1.1.2. active substance(s) not described in a pharmacopeia**

**1.2. Scintific Data**
**1.2.1. Nomenclature**
**1.2.2. Description**
**1.2.3. Manufacture**
**1.2.4. Quality control during manufature**
**1.2.5. Development**
**1.2.6. Impurities/ heavey metals**
**1.2.7. Batch analysis**

**2. Excipient(s)**
**2.1. Specification and routine tests**
**2.1.1. Excipient(s) described in a pharmacopeia**
**2.1.2. Excipient(s) not described in a pharmacopeia**

**2.2. Scientific Data**

**3- Packaging material( Immediate packaging)**
**3.1. Specification and routin tests**
**3.2. Scientific data**

**IID: Special Disposal relevant To The Prevence Of Transmission of Bovine Spongiforme Encephalopathy**
**IIE: Control Test ON Intermediate Products( If Necessary)**
**IIF: Control Tests Of Final Product**
**1. Specifications And Routine Tests**
**1.1. Product specifications and tests for release at time of manufacture( general characterstics,specific standards)**
**1.2. control methods**
**1.2.1. test procedures for identification and quantitive determination for the active substance(s)**

**2.Scientific Data**
**2.1. Analytical validation of methods and comments on the choice of routine tests and standards**
**2.2. Batch analyses**

**IIG: Stability**
**The following are the guidelines onsubmission of the stability data**
**Instractions:**
**Accelerated stability studies : Give brief description of the accelerated stability conducted to establish the effects of the increase of change f the rate of chemical degradation and physical change of adrug using exaggerated storage conditions**

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**Explanatory Notes**
**1- These studies shall be conducted at40(-,+)2/75% RH for six monthes at sampling frequency of initial 1,2,3 and 6 months in humidity chambers**
**2- The parameters to be examined , number of bathes , sampling plan , type of packing and analytical test procedures shall be similar to those under real – time stability ( see bellow)**
**3- Accelerated stability data results shall enable proposition of a tentative shelf – life of 24 months , which shall later be confirmed by completed real – time stability studies**
**4- The requirement of orientatation of containers and container closure systems is equally applicable here as is the case for real time stability studies.**

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**Real time stability studies**
**Describe briefly the real time stability studies performed to establish the shelf – life and storage condition of the product:1- Real time stability studies should be conducted under controlled conditions in stability chambers and not open shelves.**
**2- They should be carried out under zone 111 of the world climatic conditions (hot/dry) which ae fixed at 25+,-2 /65+,-5%.**
**3- sampling shuld be done at initial 3,6,9,12,18,24,36,etc.Months to establish the stability characterstics of the drug product.**
**4- sampling from three diffferent batches , which are randomly selected to represent the whole batch , should be issued for the study.**

**5- Attributes (parameters) to be tested should be those susceptible to change and are likely to influence the quality , safety and efficacy of the pharmaceutical product.**
**These parameters should be atleast cover: a: Appearance for all dosage forms**
**b: assay (stability indication )for all dosage forms**
**c: Degradation products / impurities forall dosage forms.**
**d: Physiological properties such as disintegration,hardness,particle matter etc, for all solid dosage forms**
**e: Dissolution for all solid and semi solid oral dosage forms.**
**f: Microbial limits for dosage forms**
**g: pH for liquid preparations**
**6- A description of the samling plan used to select the sampling from the test batch for storage and subsequent testing should be given .**
**7- Forliquid , dispresed systems and semi – solid products , samples should be stored in upright , horizontal and inverted position to ensure full intractins with all primary packinging materials.**

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**Provide results of stability studies for the three batces tested.**
**1.Results should be presented in tabular from or graphs (whereever possible).**
**2. acceptable crteria should be fixed for each test included in the stability study .the criteria can be in the form of numerical limits if results are quantitaive (e.g.asssay degradation products,particle size and viscosity).**
**For qualitative tests,the criteria can be pass or fail ( e.g.odour , color, appearance )**
**3. Analytical test procedures shall be fully validated and assay shall be stability indicating . For products with official monographs , the procedures in the current edition of the official compendia stipulated in these guide lines will apply.**

**1. stability tests on active substance(s)**
**2. stability tests on finished product**

**IIH:Data Related To The environmental Risk Assessment For Products containing,Or Consisting Of Generally Modified Organisms(GMOs)**

**IIQ: Other Information**

**Part III :**

**Safety And Residue Documentation The requirement for submission of safety data is applicable for products which are not official in current editions of pharmacopoeia and for herbal medicines which are not listed in the current WHO monographs on Selected Medicinal Plants.**

**- a)For products of long –term traditional use : Bibliographical ( documentary ) evidence of safety should be submitted including the following :**

**i) Evidence of long –term use ( in terms of decades)**

**ii)Specification of the system of traditional medicine, disorders treated, numbers of users and countres of use as found in literature , monographs, etc)**

**iii) Indication of the lack of toxicity poblems over the documented period of time**

**iv) If toxiciry problems are revealed by the documentation , toxicological studies should be done to determine safe dosage , and risk assessment made and presented in the dossier.**

**v) detail of the potential for misuse, abuse or dependece**

**vi) bibliographical evidence sources include reference literature (textbooks,jurnals etc),cases reports ,pharmacoeipal monographs**

**vii) In the case oflocal products where there may not be much bibliographical evidence available , the applicant should write asummary clearly confirming the safety of the product.**

**b) For foreign products where there is no bibliographi cal evidence of safety in long – term use : toxicological studies proving safety are necessary , and should be submitted in the dossier.**

**e) Non clinical studies**

**Provide full information to support safety of the herbal medicine by submitting results of the folloing tests .**

**i). acute toxicity tests using at least two species one of them being a non rudent .**

**ii). Subacute toxicity tests**

**iii). Chronic toxicity tests**

**iv). Mutagenic tests using salmonella (Ames test) or other tests**

**v). Teatogenicity tests if a product is to be administered to pregnant women**

**vi). Immune toxicity (test for allergic reactions)**

**vii).Carcinogenicity tests**
**viii).Reproductive toxicity tests**

**IIIA:Safety Ducumentation**
**IIIA1:Precies Identification Of The Product Concerned By The Application Detail Of The Active Substance(s)**
**IIIA2: Pharmacological Studies**

**IIIA3: Toxicological Studies**
**IIIA4: Studies Of Other Effects**
**IIIA5: User Safety**
**IIIB6: Ecotoxicity**
**IIIB: Residue Documentation**
**IIIB1: Precise Identification Of the Product Concerned By The Application**
**IIIB2: Residues Studies**
**IIIB3: Analytical Methods**

**Part IV:**
**Pre-Clinical And Clinical Documentation**
**Efficacy data:**
**The requirement for submission of efficacy data is applicable for products which are not official in current editions of pharmacopoeia and for herbal medicines which are not listed in the current WHO monographs on Selected Medicinal Plants. It shall be noted that only those therapeutic uses which are established thrugh clinical studies are acceptable for herbal medicines listed in the current WHO monographs on Selected Medicinal Plants.The rest of the herbal medicines shall be required to provide evidence of efficacy as outlined below.**

**a )Pharmacological and clinical effects of active ingredients and their (a active constituents if known should be described , and should be relevant to the main indications of the product**
**b)For products with long –term traditional use,used for minor disorders or non-specific indications or for prophylactic use :Bibliographic evidence of**

**efficacy should be submitted ,e.g. Literature (text books, jurnals etc),case report ,pharmacopoeial monographs**
**c)For products without bibliographical evidence of efficacy in traditional use: reports of clinical studies proving efficacy**
**d) combination products :for new combinations of active ingredients , the therapeutic justification,compatibility and dose range should be given . For well established combinations,photocopies of refrences in traditional texts (eg.Ayurveda,traditional chinese) will be acceptable as evidence of efficacy**
**e)In the case of local products where ther may be little or no bibliographical evidence available , the applicant should write a summary clearly explaining the efficacy of the product.**

**IV A: Pharmacology**
**IV A1: Pharmacodinamics**
**IV A2: PharmacoKinetics**
**IV B: Tolerance In Target Species Of Animals**
***IV C: Resistance***

تذکر۱: پرونده اطلاعتی می بایست دارای فهرست وذکر شماره صفحه باشد
تذکر۲: هرگونه اشتباه تايپي واصلاح در متن پرونده دارو(Dossier) از جمله محدوده هاي استاندارد ونتايج آزمايشات ارسالي قابل قبول نخواهد بود .
تذکر۳: گزارشات فارماکولوژي و توکسيکولوژي فقط در محل شرکت موجود باشد تا در صورت نياز به دفتر دارو و درمان ارسال گردد.

Note 1- The file must have a list and page numbers.
Note 2- Any typographical errors and corrections in the text of the file, including standard ranges and test results submitted, will not be acceptable.
Note 3- Pharmacology and toxicology reports should only be available at the company's location so that they can be sent to the Drug and Treatment Office if needed.