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# COMPARATIVE STUDY OF DOSSIER REGISTRATION PROCESS OF MULTI SOURCE HIGHLY VARIABLE DRUG PRODUCTS IN MAJOR COUNTRIES

**B Kalyani[1*], G Ramakrishna[2], M V Nagabhushanam[3]**

[1]Department of Pharmaceutical Regulatory Affairs, Hindu College of Pharmacy, Amaravathi Road, Guntur, Andhra Pradesh, India-522002.

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**Abstract:**

*In this paper we did individually study about the rule & regulations which are followed for drug approval process in USA & Europe & also we did individually study for the specific requirement of data in CTD, Paper documents for the marketing authorization of pharmaceutical products. Quality must ensure consistency of safety and efficacy during the shelf life of all batches produced. This paper summarizes here for the process of drug discovery procedure in brief & in co- ordination with the different regulatory authorities with Europe & USA and in last we did the comparative study. This comparative study of dossier compilation given a brief idea about the difference in regulatory requirements for drug approval process among USA & EU.*

**Keywords:** *Dossier Registration Process, Multi Source Highly Variable Drugs, India, USA & Europe.*

**Corresponding author:**

**B Kalyani,**

*II/II M.Pharmacy, Department of Pharmaceutical Regulatory Affairs, Hindu College of Pharmacy, Amaravathi Road, Guntur, Andhra Pradesh, India-522002.*

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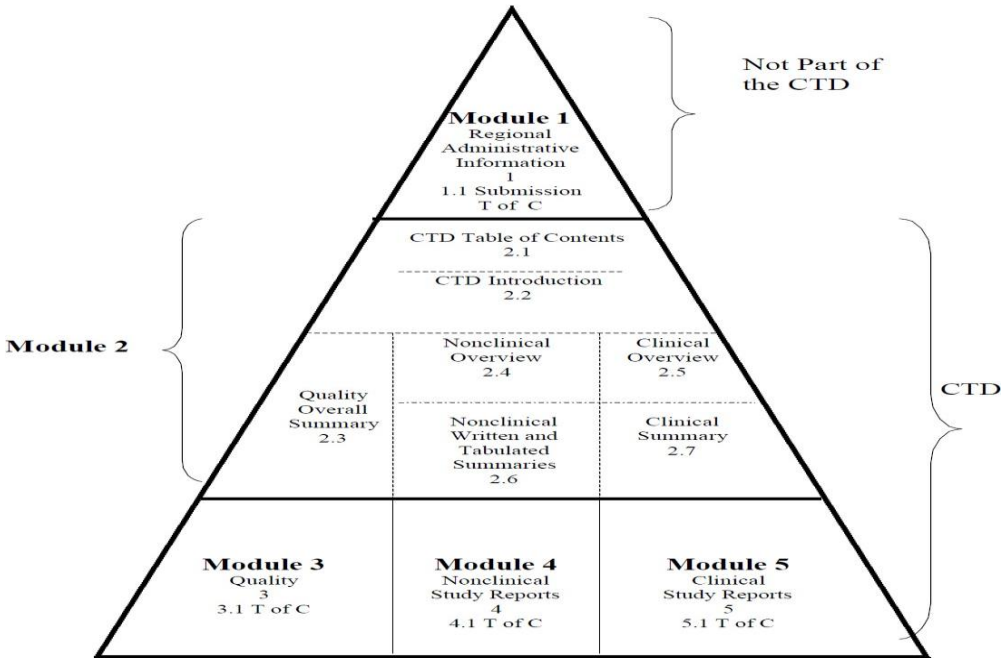
**INTRODUCTION [1-3]:**

COMMON TECHNICAL DOCUMENT (DOSSIER) Dossier is a file document submitted for the approval of new drug or drug product. It is submitted in form of CTD. CTD is a harmonized format (template) for presenting data in the ICH regions. In some countries, it is optional. The process of reviewing & assessing dossier to support a medicinal product in view of its marketing (also called licensing, registration, approval, etc.), obviously finalized by granting of a document also called marketing authorization. This process is performed within a legislative framework which defines the requirements necessary for application to the concerned (competent) regulatory authority, details on the assessment procedure (based on quality, efficacy and safety criteria) and the grounds for approval or rejection of the application, and the circumstances where a marketing authorization already granted may be withdrawn, suspended or revoked.

Dossier is a file document submitted based on the requirement of regulatory agency for the approval of drug product. It is essential to submit dossier file in the form of common technical document in USA and EUROPE.

**Diagrammatic Representation of the ICH Common Technical Document**




**Europe guideline for highly variable drug products (hvdp):**

Highly variable drug products (HVDP) are those whose intra-subject variability for a parameter is larger than 30% (Europe BA/BE CPMP/EWP/ QWP/1401/98). If an applicant suspects that a drug product can be considered as highly variable in its rate and/or extent of absorption, a replicate cross-over design study can be carried out.

Those HVDP for which a wider difference in Cmax is considered clinically irrelevant based on a sound clinical justification can be assessed with a widened acceptance range. If this is the case the acceptance criteria for Cmax can be widened to a maximum of 69.84 – 143.19%. For the acceptance interval to be widened the bioequivalence study must be of a replicate design where it has been demonstrated that the within-subject variability for Cmax of the reference compound in the study is >30%.

The applicant should justify that the calculated intra-subject variability is a reliable estimate and that it is not the result of outliers. The request for widened interval must be prospectively specified in the protocol.

**Parameter to be determined:**

For single dose study pharmacokinetic parameter Cmax, AUC0-t, AUC0-∞ residual area Tmax, Kel,

t1/2 is determined using plasma time concentration profile of drug For multiple dose studies AUC(0-t), Cmax, ss and tmax, ss determined using plasma time concentration profile of drug. (FDA BA/BE General consideration 2003).

**Statistical analysis:**
Statistical analysis will be performed on the data obtained from subjects. Descriptive statistics of all the pharmacokinetic parameters will be computed and reported. (FDA BA/BE Statistical approach 2001; Rani and Pargal, 2004)

**Ratio analysis:**
Ratio of least squares means of test and reference formulations will be computed for lntransformed pharmacokinetic parameters Cmax, AUC0-t and AUC0-∞. Ratio analysis will be reported for ln-transformed pharmacokinetic parameters Cmax, AUC0-t and AUC0-∞ for analyte. Intra-subject variability: Intra-Subject variability will be computed for ln-transformed pharmacokinetic parameters Cmax, AUC0-t and AUC0-∞ for analyte.

**Acceptance parameter for bioequivalence:**
Two one-sided tests for bioequivalence and 90% confidence intervals for the ratio of least squares mean between drug formulations will be calculated, for In-transformed data of Cmax, AUC0-t and AUC0-∞ for single dose study and AUC(0-t) and Cmax, ss for multiple dose study. In Europe and South Korea guideline suggest that if the drug having long half life and sampling duration is more than 72 hours. In this case AUC is truncated up to 72 hr and no need to measures AUC0-∞ and residual area.

**Table-1-Acceptance criteria for bioequivalence:**

| S.No | Parameter | USA | EUROPE |
|---|---|---|---|
| 1 | $C_{max}$ % | 80-125 | 80-125 |
| 2 | $AUC_{0-t}$ % | 80-125 | 80-125 |
| 3 | $AUC_{0-\infty}$ % | 80-125 | Not applicable |

## RESEARCH METHODOLOGY [4-6]:

Literature review was done mainly on the generic drug approval process in two regions, they are US and Europe. The research is carried out with the collected data by analyzing the terms of the below parameters:

**Methodology:**
Each and every study has some patterns and follows certain pathways in order to reach the destination. Thus, the method to be followed plays an important role in determining the outputs as well as consequences of the study.

**Types of study:**
The study was conducted with an objective to sketch the regulatory framework for Generic Drug Approval process in US and Europe, emphasizing on the application form, approval timelines and sequence of steps in the generic drug approval.

**Source of data:**
Major part of the data collected through the following sources but the interpretation and organization of this data collected was done to understand clearly and in an easiest way. Collection of data was done through following sources

**Literature Review:**
Typically covered the books and Regulatory guidelines published by government authorities including the academic journals, online journals, market research reports, world fact and other sources.

**Internet using the webpage content:**
The literature was collected using numerous search engines like Pharma knowledge base, Center for Pharmaceutical Information and Engineering Research (CPIER) and official Government websites like FDA and EMEA. Key words in the search involved generic drug registration requirements along

with the name of various parameters associated to pharmaceutical field, name of regulatory bodies and other variations were used. The patent information which is included in this work is obtained for the country specific patent organizations and World Intellectual Property Organization.

**Marketing authorisation process in europe and usa [5]:**

Authorisation of medicines is done by four procedures:

- Centralised Procedure
- Mutually Recognition Procedure
- Decentralised Procedure

**Comparative study of dossier submission process ofdrug product in usa & eu [6-10]:**

**Submission Related to the Administrative:**

The following requirements to be submitted for the regulatory bodies for granting market authorization. For the **European country** the application for the new drug product is submitted to marketing authorization application agency. As per the country guideline there is no need to submit patent status or debarment certificate. The document should be submitted in the eCTD format, in 1 set. Generally it takes 12 to 18 months for the approval. There is a submission feefor approval i.e. 10 to 20 lakh. Major hold up during authorization is patent infringement, GMP audit, high cost of registration, administrative procedure for each member state.

For the country **United States of America** the application for the new drug product is submitted as New Drug Application (NDA) and for the generic drugs application should be submitted as Abbreviated new Drug Application (ANDA) along with the patent status or debarment certificate. The document should be submitted in the eCTD format or paper, in 3 sets. Generallyit takes 12 to 24 months for the approval. There is no any fee for the submission. Major hold up during authorization is patent infringement, FDA audit, competition.

**Submission Related to Stability:**

Following tables illustrates the stability zone as per the ICH guidelines and different guidelines to maintain the stability requirement in different country. As per the survey by several countries/ regions have revised their own stability testing guidelines for larger safety margin (e.g. 30°C/75%RH as long-term storage condition) so for this reason ICH Q1F –For Zones III and IV (Hot & Dry or Hot & Humid) have withdrawn in June 2006. Impact of this change on ICH Q1A (R2) is that intermediate testing condition is unchanged: 30°C/65% RH. On the decision of useof applicant 30°C/75% RH is acceptable.

**Table-2-COMPARISON OF REGULATORY REQUIREMENT BETWEEN USA AND EUROPE**

| ADMINISTRATIVE | | |
|---|---|---|
| **Requirement** | **USA** | **EU** |
| Application | ANDA | MAA |
| Approval Time line | 18 Month | 12 Month |
| Copies | 3 (archival, review, field) | 1 |
| Debarment certification | Required | Not required |
| Pharmacovigilance | Not required | Required |
| Agent Authorization | Required | Not required |
| **MANUFACTURING AND CONTROL** | | |
| **Requirement** | **USA** | **EU** |
| Batch size | 1 pilot scale or 1 lakh units | 2 pilot scale + 1 lab batch or minimum 1 lakh units |
| Packaging | Minimum 1 lakh units | Not required |
| Process validation | Not required at the time ofsubmission | Required if it is MR formulation or aseptic product |

| FINISH PRODUCT CONTROL | | |
|---|---|---|
| **Requirement** | **USA** | **EU** |
| Assay | 90-100% | 95-105% |
| Identification Test | Single test | Additional test required |
| Color identification | Not required | Required |
| Water content | Required | Not required |
| Disintegration test | Not required | Required |
| **LABELING REQUIREMENT** | | |
| **Requirement** | **USA** | **EU** |
| NDC No. | Required (10 digit) | Not required |
| Prescription status | $R_X$ | POM (Prescription only medicines) |
| Labels | Vials/ Carton/ PIL | Vials/ Carton/ PIL/SPC |
| Side by side comparison | Vials/ Carton/ PIL | Not required |
| Readability testing | Not required | Required |
| QP Certification | Not required | Required |
| **STABILITY REQUIREMENT** | | |
| **Requirement** | **USA** | **EU** |
| No. of batches | 1 | 2 |
| Date and time of submission | 3 Months accelerated and 3 months long term | 6 Months accelerated and 6 months long term |
| Container orientation | Inverted and upright | Do not addressed |
| **BIOEQUIVALENCE REQUIREMENT** | | |
| **Requirement** | **USA** | **EU** |
| CRO | Audited by FDA | Audited by MHRA |
| Reserve Sample | 5 times the sample requiredfor analysis | No such requirement |
| Fasted/ Fed | Fasting, fed and steady state | Fasting is required |
| Retention of samples | 5 years from the date offilling the application | No such requirement but usually followed |
| Biowaiver criteria | Wt. Proportionate/ Wt. similar/ SUPAC level III | Wt. Proportionate/ Wt. similar |

**Bioavailability:**

Bioavailability is a measurement of the extent of a therapeutically active medicine that reaches the systemic circulation and is therefore available at the site of action. For most medicines that are taken orally, the active ingredients are released in the gastrointestinal (GI) tract and arrive at their site of action via the systemic circulation. Blood concentrations of the active ingredients and/or their active metabolites thereby provide a marker for the concentration at the site of action and a valid measure of bioavailability. A blood concentration – time curve (achieved by serial measurements over time) reflects not just the release of the active

ingredient from the medicine and its absorption from the GI tract, but also other factors including presystemic metabolism, distribution and elimination. Bioavailability is assessed using three main pharmacokinetic variables.
Area under the blood drug concentration versus time curve (AUC) Maximum blood concentration (Cmax)
Time to reach maximum concentration (Tmax)

**Bioequivalence:**
If two medicines are bioequivalent there is no clinically significant difference in their bioavailability. Although bioequivalence is most commonly discussed in relation to generic medicines, it is important to note that bioequivalence studies are also performed for innovator medicines in some situations such as:

A. Between early and late clinical trial formulations or between the formulations used in clinical trials and the product to be marketed for new medicines.

B. When changes in formulation have occurred after an innovator product has been approved, for example a change in one or more excipients (inactive ingredients).

Bioequivalence studies are a surrogate marker for clinical effectiveness and safety data as it would not normally be practical to repeat clinical studies for generic products. It is accepted that if plasma concentrations of the active ingredient of the generic and innovator medicines are the same, then their concentration at the site of action and therefore their safety and effectivenesswill be the same. In addition to being bioequivalent, a generic medicine must conform to high quality standards in terms of the method of manufacture and the purity of the final pharmaceutical form. There are internationally agreed standards for measuring and assessing bioequivalence.
Acceptance Criteria for Bioequivalence.

Bioequivalence is determined based on the relative bioavailability of the innovator medicine versus the generic medicine. It is measured by comparing the ratio of the pharmacokinetic variables for the innovator versus the generic medicine where equality is 1.

**Table-3-COMPARISON OF REGULATORY REQUIREMENT BETWEEN USA AND EUROPE**

| **ADMINISTRATIVE** | | |
|---|---|---|
| **Requirement** | **USA** | **EU** |
| Application | ANDA | MAA |
| Approval Time line | 18 Month | 12 Month |
| Copies | 3 (archival, review, field) | 1 |
| Debarment certification | Required | Not required |
| Pharmacovigilance | Not required | Required |
| Agent Authorization | Required | Not required |
| **MANUFACTURING AND CONTROL** | | |
| **Requirement** | **USA** | **EU** |
| Batch size | 1 pilot scale or 1 lakh units | 2 pilot scale + 1 lab batch or minimum 1 lakh units |
| Packaging | Minimum 1 lakh units | Not required |
| Process validation | Not required at the time ofsubmission | Required if it is MR formulation or aseptic product |
| **FINISH PRODUCT CONTROL** | | |
| **Requirement** | **USA** | **EU** |
| Assay | 90-100% | 95-105% |
| Identification Test | Single test | Additional test required |

| | | |
|---|---|---|
| Color identification | Not required | Required |
| Water content | Required | Not required |
| Disintegration test | Not required | Required |
| **LABELING REQUIREMENT** | | |
| **Requirement** | **USA** | **EU** |
| NDC No. | Required (10 digit) | Not required |
| Prescription status | $R_X$ | POM (Prescription only medicines) |
| Labels | Vials/ Carton/ PIL | Vials/ Carton/ PIL/SPC |
| Side by side comparison | Vials/ Carton/ PIL | Not required |
| Readability testing | Not required | Required |
| QP Certification | Not required | Required |
| **STABILITY REQUIREMENT** | | |
| **Requirement** | **USA** | **EU** |
| No. of batches | 1 | 2 |
| Date and time of | 3 Months accelerated and 3 | 6 Months accelerated and 6 |

**EUROPE GUIDELINE FOR HIGHLY VARIABLE DRUG [10-12]:**

Highly variable drug products (HVDP) are those whose intra-subject variability for a parameter is larger than 30% (Europe BA/BE CPMP/EWP/ QWP/1401/98 Rev. 1/ Corr*). If an applicant suspects that a drug product can be considered as highly variable in its rate and/or extent of absorption, a replicate cross-over design study can be carried out. Those HVDP for which a wider difference in $C_{max}$ is considered clinically irrelevant based on a sound clinical justification can be assessed with a widened acceptance range. If this is the case the acceptance criteria for $C_{max}$ can be widened to a maximum of 69.84 – 143.19%. For the acceptance interval to be widened the bioequivalence study must be of a replicate design where it has been demonstrated that the within-subject variability for $C_{max}$ of the reference compound in the study is >30%. The applicant should justify that the calculated intra-subject variability is a reliable estimate and thatit is not the result of outliers. The request for widened interval must be prospectively specified in the protocol.

**Parameter to be determined:**

For single dose study pharmacokinetic parameter $C_{max}$, $AUC_{0-t}$, $AUC_{0-\infty}$ residual area $T_{max}$, Kel, $t_{1/2}$ is determined using plasma time concentration profile of drug For multiple dose studies AUC(0-t), $C_{max,ss}$ and $t_{max,ss}$ determined using plasma time concentration profile of drug. (FDA BA/BE General consideration 2003).

**Statistical analysis:**

Statistical analysis will be performed on the data obtained from subjects. Descriptive statistics of all the pharmacokinetic parameters will be computed and reported. (FDA BA/BE Statistical approach 2001; Rani and Pargal, 2004).

**Analysis of variance (ANOVA):**

The ln-transformed pharmacokinetic parameters $C_{max}$, $AUC_{0-t}$ and $AUC_{0-\infty}$ of analyte will be subjected to Analysis of Variance (ANOVA). ANOVA model will include Sequence, Formulation and Period as fixed effects and Subject (Sequence) as a random effect. Sequence effect will be tested using Subject (Sequence) as error term. The significance of the sequence effect at alpha 0.10 will be tested using the subjects nested within the sequence as the error term.

An F-test will be performed to determine the statistical significance of the effects involved in the model at a significance level of 5% (alpha =0.05).

**Power:** The power of a test to detect 20% difference between test and reference formulations will be computed and reported.

**Ratio analysis:**

Ratio of least squares means of test and reference formulations will be computed for ln- transformed

pharmacokinetic parameters Cmax, $AUC_{0-t}$ and $AUC_{0-\infty}$.

Ratio analysis will be reported for ln-transformed pharmacokinetic parameters Cmax, $AUC_{0-t}$ and $AUC_{0-\infty}$ for analyte.

**Intra-subject variability:**

Intra-Subject variability will be computed for ln-transformed pharmacokinetic parameters Cmax, $AUC_{0-t}$ and $AUC_{0-\infty}$ for analyte.

**Acceptance parameter for bioequivalence:**

Two one-sided test for bioequivalence and 90% confidence intervals for the ratio of least squares mean between drug formulations will be calculated, for In-transformed data of Cmax, $AUC_{0-t}$ and $AUC_{0-\infty}$ for single dose study and $AUC_{(0-t)}$ and $C_{max,ss}$ for multiple dose study.

In Europe and South Korea guideline suggest that if the drug having long half life and sampling duration is more than 72 hours. In this case AUC is truncated up to 72 hr and no need to measures $AUC_{0-\infty}$ and residual area. [26]

**Table-4-Acceptance criteria for bioequivalence:**

| S.No | Parameter | USA | EUROPE |
|---|---|---|---|
| 1 | Cmax % | 80-125 | 80-125 |
| 2 | $AUC_{0-t}$ % | 80-125 | 80-125 |
| 3 | $AUC_{0-\infty}$ % | 80-125 | Not applicable |

**Table-5-The tables given below consist of the possible regulatory requirements for the registrationapplication as per US and European regulatory guidelines:**

| S.NO | USFDA | EUROPE |
|---|---|---|
| **I** | **General** | |
| **1** | **FDA** is the sole regulatory authority forcontrolling and regulating the food and drugs. | **EMEA** is the centralized authority and many CPMP, MHRA, CHMP etc. countrywise for the approval of the market authorization application in whole Europe. |
| **2** | The eCTD is mandatory for the submissionof the drug applications (NDA/ANDA) | The eCTD is not fully mandatory but NeeS is submitted along with the paper submission for MAA till end of December 2009. |
| **3** | US FDA guidance (CFR) documents andFDA sections (e.g. 505 (b) for NDA and 505(j) for ANDA)15 are followed for the preparation of the dossier for the drug approval applications. | Expert reports and Directives (e.g. Directive 2001/83/EC-Article 8(j))16drafted are followed in making the dossiers for market authorization application |
| **4** | The applications are different e.g.For new drug- NDA<br>For generic drug – ANDA<br>For biological application – BLA | Only single type of application is applicable for each new drug, generic drug etc is MAA (Market Authorization Application). |

| | | |
|---|---|---|
| **5** | The application is directly submit to theFDA by the applicant or through any approved contact agent for whom a certification is provided to the agency according to the GDEA 199217. | Three processes for drugs approval are applicable in Europe11<br>A) Centralized procedure (CP)<br>B) Decentralized procedure (DCP)/ Mutual Recognition procedure(MRP)<br>C) National procedures |
| **6** | The technical data about drug substance orAPI is known as DMF (Drug Master File Type II) and is submitted in the eCTD inModule 2 **(2.3.S)** and 3 **(3.2.S).** | The technical data about drug substance submitted with the dossier in 2.3.S and 3.2.S part of the eCTD is known as ASMF(Active Substance Master File). |
| **7** | CFN (Central file no.) or FEI no. is submitted to FDA which is issued by thedistrict government. | No any CFN or FEI no. is submitted to theagency. |

| S.NO | USFDA | EUROPE |
|---|---|---|
| **II** | **Module 1:Regional information** | |
| **1** | Administrative information is different i.e.cover letter, forms (356h), application information, field copy certification, debarment certification, financial certification, Patent information and exclusivity18. | Administrative information such as coverletter specified for the particular country, application form applicable in that country, exclusivity statement, proof of Payment to clinical investigators, proof of establishment of the applicant in EEA. |
| **2** | The paper size for the submission is Lettersize (8.5x11 inches) with font size 12 in times new roman format. The tables and figures have small font size i.e. 8 to 10. | A4 (8.27x11.69inches) paper size is usedfor the dossier preparation with font size 12 in times new roman format. |
| **3** | Package inserts are provided for drugproduct in labeling. | SPC (summary of product characteristic)19 is provided about thedrug product in labeling. |
| **4** | Proposed Labels and cartons with proper dimensions similar to that of the RLD labelsare provided. | Mock ups and specimens of labels andcartons sent with the application as appropriate. Braille is used for the labeling conditions on the labels. |
| **5** | The information about the clinical investigators is provided in the Module 5and in financial disclosure Statement section of this module. | The information (curriculum vitae) of the experts (Quality and Clinical) is provided. |
| **6** | Request for waiver of in-vivo BE studies is provided in the module 1. | Request for waive is not provided in the module 1. |
| **7** | Annotated draft labeling (side by side) for labels and cartons compared with the RLD with proper annotation is provided. | No annotation (side by side) for labeling is provided. Everything is provided in the SPC and package inserts. |

| | | |
|---|---|---|
| **8** | The EAS (Environment Assessment Statement20) for categorical exclusion certification in compliance with the law of EPA of US is provided. | Environ risk Certification21 is given with the information for GMO or Non - GMO. The fresh/new certificate is provided. |
| **9** | Risk management Plans section is forthe post marketing surveillance and controlling the adverse effects of the drugsby proper management. This is the part of Clinical Trial Phase IV. | A separate additional section is providedfor the pharmacovigilance system for surveying and controlling the post approval undesired effects of the drug. |

| S.NO | USFDA | EUROPE |
|---|---|---|
| **10** | **Module 3.2.R** | |
| **i.** | The executed batch records for manufacturing and packaging are providedin Module 3.2.R for only single batch. | The three executed batch records for manufacturing and packaging for process validation schemes are provided in Module 3.2.R. |
| **ii.** | The declaration is given for the residual solvents limits used or present in the drugsubstance and excipients according to theUSP <467>[22]. | The declaration is given for the residual solvents limits used or present in the drugsubstance and excipients accordance withthe ICH limit mention in the Q3C (R3) impurities[23] |
| **iii.** | Information on components including the name and address of the supplier or manufacturer of the raw material, packagematerial etc provided in the 3.2.R. | information in components employed in the drug product formulations is generallynot provided in the module 3.2.R |
| **iv.** | Letter of Access is not mentioned in 3.2.R. | Letter of access to Active substance master file of drug substance is provided for the agency. |
| **v.** | TSE and BSE certificates are not attachedin this section whereas submit in DMF. | TSE and BSE certificates are attached fordrug substance and excipients. |
| **vi.** | Certificate of suitability (CEP certificate) isnot applicable. | The latest Certificate of suitability (CEP)24 obtained from the EDQM Europe for each drug substance and excipients are attached. |
| **vii.** | Comparability protocols are not attached forboth the drug substance and drug products. | Comparability protocols are attached. A comparability protocol prospectively specifies the tests and studies that will be performed, analytical procedures that willbe used, and acceptance criteria that will be achieved to assess the effect of CMC changes25. |
| **III** | **Other Differences** | |
| **i.** | Node extension is not allowed in the eCTD XML in software. | Node extension can be permissible. |

| | | |
|---|---|---|
| **ii.** | Structured product labeling (SPL)26 and study tagging file (STF)27 is mandatory bythe USFDA in eCTD of a drug registration application. Paper CTD format is not accepted by FDA at all. | SPL and STF are not applicable in European eCTD dossier preparation because it not fully mandatory in Europe. NeeS21 format is submitted in place ofeCTD along with paper CTD dossier. |

## SUMMARY AND CONCLUSION:

### SUMMARY:

In this paper we did individually study about the rule & regulations which are followed for drug approval process in USA & Europe. Also we did individually study for the specific requirement of data in CTD/Paper documents for the marketing authorization of pharmaceutical products. Data in the dossier gives the answer of following questions: What is the product? Is the quality presented acceptable on grounds of safety and efficacy? Is the quality presented reproducible? How long can the quality be maintained? Quality must ensure consistency of safety and efficacy during the shelf life of all batches produced.

This paper summarizes here for the process of drug discovery procedure in brief & in co- ordination with the different regulatory authorities with Europe & USA.

And in last we did the comparative study. This comparative study of dossier compilation given a brief idea about the difference in regulatory requirements for drug approval process among USA & EU.

### CONCLUSION:

Here we conclude that the CTD and eCTD significantly reduces the time and resources needed to compile applications for registration of human pharmaceuticals. Eases the preparation of electronic submissions. Facilitates regulatory reviews and communication with the applicant by a standard document of common elements. Simplifies exchange of regulatory information between Regulatory Authorities etc.

Provide for a scientifically sound means of establishing the quality, safety and efficacy of therapeutic products. Improve the transparency, predictability and efficiency of the regulatory process. Contribute to reducing unnecessary regulatory burden and promoting industry compliance. Promote bilateral and multilateral regulatory communication and cooperation – common regulatory platform. Level playing field good for export market.

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