statistical confidence. However, non-inferiority design may be considered where relevant (given adequate and scientific/ethical justification).

ix. Depending on the claim, superiority or non-inferiority should be demonstrated for each specified clinical outcome. For example, if the claim for the FDC is "less bone marrow depression", and similar efficacy as compared to the one or more of the actives, a non-inferiority outcome should be demonstrated for efficacy and a superiority outcome for safety.

x. In clinical trials that are intended to test for superiority and/or non-inferiority, the choice of comparator should be carefully considered and will depend in part on the medical and ethical circumstances. The comparator may be:

   a. The treatment whose risk–benefit profile is best supported by evidence or is at least well established.
   b. One or more of the actives in the FDC given as a single treatment.
   c. A placebo (where scientifically needed and ethically justified).

xi. In the context of FDCs, equivalence trials are largely confined to bioequivalence studies.

xii. If the combination is intended for long-term use, data on safety in patients will normally be required for 6 months or longer.

xiii. End-points in clinical trials should be such as to characterize the advantages and disadvantages of the combination. For example, for a combination designed to reduce the development of drug resistance, end-points might include the frequency of new drug resistance as well as the overall clinical outcome.

xiv. Multi factorial designs and parallel group comparisons are useful means by which it may be possible to demonstrate that a combination is superior to the individual actives.

xv. In some cases, studies have to be specifically designed to confirm the minimal effective dose and the usual effective dose of the combination. Multiple dose-effect studies may be necessary.

xvi. Analysis of results should discuss both the **statistical significance** and **clinical relevance**.

Annexure 7

7.1 Conduct of Bioavailability (BA)/Bioequivalence (BE) studies

General

- The CDSCO Guidelines for Bioavailabilty and Bioequivalence Studies, 2005 (available at www.cdsco.nic.in) should be referred for design and conduct of all studies
- Bioequivalence studies are required for FDCs in category
    - IIA,
    - IIB,
    - *in vitro* data for IIIA,
    - IIIB and
    - IV
- Data on absolute bioavailability shall be required in category I and III, i.e. comparison of the area under the curve for plasma concentration over time after an intravenous injection with that after administration of the dosage form to be marketed, for example a tablet given orally

Study design

1. Studies should be designed as described in CDSCO Guidelines for Bioavailabilty and Bioequivalence Studies, 2005.

2. Typically, for an FDC, a two-period, two-sequence crossover design is the design of choice with the two phases of treatment separated by an adequate washout period (components of the FDC are given together followed by FDC and *vice versa*) which should ideally be equal to or more than five half lives of the moiety with the longest half life.

3. If it is known with certainty (e.g. from published data) that the any one of the products is affected by food, then a BA/BE study in fed state is also required.

Choice of the comparator

1. The comparator should be of known quality, safety and efficacy.
2. For an FDC belonging to category IV, it should be compared to the brand that was first marketed in India for which safety and efficay is available. If more than one similar FDC is available, and the choice of comparator is NOT the first marketed FDC, this should be justified by cogent argument and data.
3. For an FDC belonging to the category IIA the comparator should be the FDC that is marketed abroad.
4. For an FDC belonging to the categories IIB/IIIB, single entity products will have been used in the majority of pivotal clinical trials. The same brands of those single entity products should be the comparator and should be given concurrently as was the case in the pivotal clinical trials.

Conditions when Biowaivers can be granted

Biowaiver will be granted as per CDSCO Guidelines for Bioavailabilty and Bioequivalence Studies, 2005 (available at www.cdsco.nic.in) – where all conditions are met by all the components of the FDC.

7.2 STRUCTURE, CONTENTS AND FORMAT FOR BIOEQUIVALENCE (BE)/ BIOAVAILABILITY (BA) STUDY REPORT

1. Title Page

- Title of the study, the protocol code
- Name of the investigational product tested, development Phase, indication studied
- A brief description of the trial design,
- the start and end date of patient accrual
- the start and end date of sample analysis
- The names of the Sponsor and the participating Institutes (Investigators).
- Names and batch numbers of the products compared

2. A signed declaration that the test product was identical to that intended for marketing.
3. Study Synopsis (1 to 2 pages):

- A brief overview of the study from the protocol development to the trial closure should be given here.
- This section will only summarize the important conclusions derived from the study.

4. Statement of compliance with the 'Guidelines for Clinical Trials on Pharmaceutical Products in India – GCP Guidelines' issued by the Central Drugs Standard Control Organization, Ministry of Health, Government of India.

5. List of Abbreviations and Definitions

6. Table of contents

7. Ethics:

- This section should document that the study was conducted in accordance with the ethical principles of Declaration of Helsinki.
- A detailed description of the Ethics Committee constitution and date(s) of approvals of trial documents for each of the participating sites should be provided.

- A declaration should state that EC notifications as per Good Clinical Practice Guidelines issued by Central Drugs Standard Control Organization, Ethical Guidelines for Biomedical Research on Human Subjects, issued by Indian Council of Medical Research and all current amendments of Schedule Y have been followed.
- EC registration numbers given by CDSCO of all the IRBs that gave ethical oversight to this study
- Ctri registration number

8. Study Team:

Briefly describe the administrative structure of the study (Investigators, site staff, Sponsor/ designates, Central laboratory, Laboratory where sample analysis was performed including the team responsible for analysis etc.).

9. Introduction:

- A brief description of the product development rationale (emphasizing the rationale for making the FDC) should be given here.
- Results of assays and other pharmaceutical tests (e.g., physical description, dimensions, mean weight, weight uniformity, comparative dissolution) carried out on the batches of products compared

10. Study Objective:

A statement describing the overall purpose of the study and the primary and secondary objectives to be achieved should be mentioned here.

11. Investigational Plan:

This section should describe the overall trial design, the Subject selection criteria, the treatment procedures, blinding / randomization techniques if any, allowed/ disallowed concomitant treatment, the data quality assurance procedures and the statistical methods planned for the analysis of the data obtained.

Details of analytical methods used, and criteria for accepting or rejecting assay results

Sampling schedules

Details of how pharmacokinetic parameters will be calculated

12. Trial Subjects

- A clear accounting of all trial Subjects who entered the study will be given here.
- Mention should also be made of all cases that were screened, randomised, and prematurely discontinued (including the reasons) e.g. consent refusals, consent withdrawals; patients withdrawn by PI for safety concerns or lack of response, protocol deviations, Deviations of the actual times from the scheduled and any other.
- Enumerate the reasons for dropouts if any
- State reasons for premature discontinuation of therapy in each applicable case.

13. Results and Statistics

a. Sample size calculation
b. Randomization schedule
c. ANOVA for AUC0-t, AUC0-∞, Cmax
d. Inter-subject, intra-subject and/or total variability if possible
e. Confidence intervals for AUC0-t, AUC0-∞, Cmax, Confidence interval (CI) values which **should not** be rounded off: therefore, to pass a CI range of 80 to 125, the values should be at least 80.00 and not more than 125.00
f. Geometric mean, arithmetic mean, ratio of means for AUC0-t, AUC0- ∞, Cmax
g. Partial AUC, only if it is used
h. Cmin, Cmax, Cpd, AUC0-τ, degree of fluctuation [(Cmax - Cmin)/Cav] and swing [(Cmax - Cmin)/Cmin], if steady state studies are employed.
i. Outliers if any including justification for omission of data with justification

14. Safety Evaluation

A list of serious adverse events, whether expected or unexpected andunexpected adverse events whether serious or not (compiled from data submitted to Licensing Authority as per Appendix XI of Schedule Y) should be included

The comparison of adverse events across study groups may be presented in a tabular or graphical form.

This section should also give a brief narrative of all important events considered related to the investigational product.

15. Discussion and overall Conclusion

Discussion of the important conclusions regarding BA and BE derived from the study including limitations.

16. List of References
17. Appendices

List of Appendices to the Clinical Trial Report

A. Protocol and amendments
B. Specimen of Case Record Form
C. Investigators' name(s) with contact addresses, phone, email etc.
D. Details of facility where study was performed
E. Details of laboratory where sample analysis was performed
F. Patient data listings including demographics
G. List of trial participants (including name and address) treated with investigational product
H. Discontinued participants
I. Protocol deviations including deviations of the actual times of sample collection from the scheduled time
J. CRFs of cases involving death and life threatening adverse event cases
K. Full validation data, quality control data
L. Representative chromatograms covering the whole concentration range for all, standard and quality control samples as well as specimens analyzed
M. Publications from the trial
N. Important publications referenced in the study
O. Audit certificate, if available

P. Investigator's certificate that he/she has read the report and that the report accurately describes the conduct and the results of the study.

- Documentation related to statistical analysis:

    a) Randomization schedule

    b) Volunteer wise plasma concentration and time points for test and reference products

    c) Volunteer wise AUC0-t, AUC0-∞, Cmax, Tmax, Kel, and t1/2 for test and reference products

    d) Logarithmic transformed measures used for BE demonstration

    e) ANOVA for AUC0-t, AUC0-∞, Cmax

Annexure 8

Pharmacokinetic Studies

1. In general, it is desirable that there be no pharmacokinetic or pharmacodynamic interactions between the components of a FDC.
2. However, there are circumstances in which such an interaction is intentional and may even contribute to the therapeutic outcome. For example:

    a. Ritonavir boosts the activity of protease inhibitors.

    b. Carbidopa and benserazide both reduce decarboxylation of levodopa in the gut wall, and consequently reduce the dose of levodopa that should be administered.

    c. Clavulanic acid reduces bacterial hydrolysis of betalactam antibiotics and consequently both increases the concentration and prolongs the duration of effectiveness.

3. Tests should be conducted to elucidate any pharmacokinetic or pharmacodynamic interaction between the actives in a combination.

4. Some interactions may be predictable from pharmacokinetic and enzyme profiles, but should be confirmed by experiment.

5. Any interaction should be quantified so that its effect on safety and efficacy is either predictable or (preferably) has been tested in a clinical study.

6. This includes competing metabolic effects and effects on gastrointestinal efflux mechanisms or on renal excretion or reabsorption. Interactions may be additive, synergistic or antagonistic.

7. If there is an unintended pharmacokinetic interaction between the actives, it should be demonstrated that the therapeutic advantages of the combination outweigh any disadvantages resulting from the interaction.

8. Relevant argument and cross-references to data should be included in the section that discusses the balance between the advantages and disadvantages of the combination.

Category I

1. Form 44
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7 Risk–benefit assessment of combination. ☐
8. Regulatory approval for the individual APIs (if applicable) ☐
9. Free sale certificate from the country of origin (if applicable) ☐
10. Complete chemical and pharmaceutical data of the FDC ☐
11. GMP certification of sites of manufacture ☐
12. Proposed specifications and Certificate of analysis of study drug(s) ☐
13. Copy of proposed Package Insert ☐
14. All Non clinical and clinical study reports (as per Appendix 2 of Schedule Y) ☐
15. Any other ☐

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Category I Exception

1. Form 44 ☐
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7. Risk–benefit assessment of combination. ☐
8. Regulatory approval for the individual APIs and the FDC ☐
9. Free sale certificate from the country of origin ☐
10. Complete chemical and pharmaceutical data ☐
11. GMP certification of sites of manufacture ☐
12. Proposed specifications and Certificate of analysis of study drug(s) ☐
13. Copy of package inserts and promotional literature ☐
14. Copy of proposed Package Insert ☐
15. Non clinical, Phase I, II & III (as per Appendix 2 of Schedule Y) ☐
16. Waiver for Phase I and Phase II approval for DCGI (if applicable) ☐
17. Any other ☐

Category IIA

1. Form 44 ☐
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7. Risk–benefit assessment of combination. ☐
8. Regulatory approval for the FDC ☐
9. Free sale certificate from the country of origin ☐
10. Complete chemical and pharmaceutical data ☐
11. GMP certification of sites of manufacture ☐
12. Proposed specifications and Certificate of analysis of study drug(s) ☐
13. Copy of package inserts and promotional literature ☐
14. Copy of proposed Package Insert ☐
15. Reports of bioequivalence studies (as per section 7.2 of the annexure 7) done as per annexure 7 ☐
16. Acute and sub acute toxicity data in case of injectable formulation ☐
17. Any other ☐

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Category IIB

1. Form 44 ☐
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7. Risk–benefit assessment of combination. ☐
8. Regulatory approval for individual API ☐
9. Free sale certificate from the country of origin ☐
10. Complete chemical and pharmaceutical data ☐
11. GMP certification of sites of manufacture ☐
12. Proposed specifications and Certificate of analysis of study drug(s) ☐
13. Copy of proposed Package Insert ☐
14. Acute and sub acute toxicity data in case of injectable formulation ☐
15. Any other ☐

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Category IIIA

1. Form 44 ☐
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7. Risk–benefit assessment of combination ☐
8. Regulatory approval for the individual API ☐
9. Free sale certificate from the country of origin ☐
10. Complete chemical and pharmaceutical data ☐
11. GMP certification of sites of manufacture ☐
12. Proposed specifications and Certificate of analysis of study drug(s) ☐
13. Copy of the package inserts and promotional literature ☐
14. Copy of proposed Package Insert ☐
15. Reports of bioequivalence studies (as per section 7.2 of the annexure 7) done as per annexure 7 ☐
16. *Invitro* studies data conducted as per CDSCO guidelines (if applicable) ☐
17. Acute and sub acute toxicity data in case of injectable formulation ☐
18. Any other ☐

Category IIIB

1. Form 44 ☐
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7. Risk–benefit assessment of combination ☐
8. Regulatory approval for the individual APIs ☐
9. Free sale certificate from the country of origin ☐
10. Complete chemical and pharmaceutical data ☐
11. GMP certification of sites of manufacture ☐
12. Proposed specifications and Certificate of analysis of study drug(s) ☐
13. Copy of proposed Package Insert ☐
14. Reports of bioequivalence studies (as per section 7.2 of the annexure 7) done as per annexure 7 ☐
15. *Invitro* studies data conducted as per CDSCO guidelines (if applicable) ☐
16. Acute and subacute toxicity data in case of injectable formulation ☐
17. Any other ☐

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Category IV

1. Form 44 ☐
2. Treasury Challan ☐
3. Justification with a valid therapeutic rationale as per Annexure 1 ☐
4. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
5. Strategies towards PMS as per Annexure 4 ☐
6. Scientific literature supporting claim as per Annexure 2 ☐
7. Risk–benefit assessment of combination. ☐
8. Regulatory status of the FDC ☐
9. List of companies marketing the FDC ☐
10. Free sale certificate from the country of origin ☐
11. Complete chemical and pharmaceutical data ☐
12. GMP certification of sites of manufacture ☐
13. Proposed specifications and Certificate of analysis of study drug(s) ☐
14. Copy of package inserts and promotional literature ☐
15. Copy of proposed Package Insert ☐
16. Reports of bioequivalence studies (as per section 7.2 of the annexure 7) done as per annexure 7 ☐
17. Acute and subacute toxicity data in case of injectable formulation ☐
18. Any other ☐

Checklist for permission to conduct clinical trials

A. Data Common to All phases of Clinical Trial

16. Form 44 ☐
17. Treasury Challan ☐
18. Application in Form -12 along with T-Challan of requisite fees (in case of import of investigational products) ☐
19. Justification with a valid therapeutic rationale as per Annexure 1 ☐
20. Source of bulk drugs /raw materials (Manufacturing license/consent letter from the approved source regarding supply of material. ☐
21. Strategies towards PMS as per Annexure 4 ☐
22. Scientific literature supporting claim as per Annexure 2 ☐
23. Risk–benefit assessment of combination. ☐
24. Regulatory approval for the individual APIs ☐
25. Free sale certificate from the country of origin ☐
26. Complete chemical and pharmaceutical data ☐
27. GMP certification of sites of manufacture ☐
28. Proposed specifications and Certificate of analysis of study drug(s) ☐

B. Data requirement specific to the Phase of Study

a. <u>Phase I Clinical Trials</u>

1. Animal Pharmacology ☐
   a. Summary ☐
   b. Data on specific pharmacological actions ☐

c. Data on general pharmacological actions

d. Data on follow-up and Supplemental Safety Pharmacology Studies ☐

e. Pharmacokinetics data ☐

2. Animal Toxicology ☐

a. General Aspects

b. Systemic Toxicity Studies ☐

i. Data of single dose toxicity studies ☐

ii. Data of dose Ranging Studies

iii. Data of repeat-dose systemic toxicity studies ☐

c. Data on Male Fertility Study

d. Data on Segment I [female fertility] Female Reproduction and Developmental Toxicity Studies ☐ ☐

e. Data on local toxicity with proposed route of clinical application (duration depending on proposed length of clinical exposure) ☐

f. Data on allergenicity/Hypersensitivity (when there is a cause for concern or for parenteral drugs, including dermal application)

g. Data on photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential) ☐ ☐

h. Data on *in vitro* genotoxicity

3. The Proposed Protocol for Conducting The Clinical Trial ☐

4. Investigator's Brochure ☐

5. Patient Information Sheet and Informed Consent Form (ICF) as per Appendix V of Schedule Y ☐

6. Copy of 'Ethics Committee' approval letters (if available) ☐

7. Registration number of Ethics Committee/s that will oversee the trial ☐

8. Case Record Form (CRF) ☐

9. Undertaking by Investigator(s) as per Appendix VII of Schedule Y and CV ☐

10. Undertaking by Sponsor(s) ☐

b. <u>Phase II Clinical Trials</u>

1. Animal Pharmacology

f. Summary ☐

a. Data on specific pharmacological actions ☐

b. Data on general pharmacological actions

c. Data on follow-up and Supplemental Safety Pharmacology Studies ☐

d. Pharmacokinetics data ☐

2. Animal Toxicology ☐

a. General Aspects

b. Systemic Toxicity Studies ☐

i. Data of single dose toxicity studies ☐

ii. Data of dose Ranging Studies

iii. Data of repeat-dose systemic toxicity studies ☐

c. Data on Male Fertility Study

d. Data on Segment I & segment II [female fertility] Female Reproduction and Developmental Toxicity Studies ☐

e. Data on local toxicity with proposed route of clinical application (duration depending on proposed length of clinical exposure) ☐

f. Data on allergenicity/Hypersensitivity (when there is a cause for concern or for parenteral drugs, including dermal application) ☐

g. Data on photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential) ☐

h. *Data on in vitro* genotoxicity ☐

3. Clinical study report of Phase I study ☐
4. The Proposed protocol for conducting the clinical trial ☐
5. Investigator's Brochure ☐
6 Patient Information Sheet and Informed Consent Form (ICF) as per Appendix V of Schedule Y ☐
7. Copy of 'Ethics Committee' approval letters (if available) ☐
8. Registration number of Ethics Committee/s that will oversee the trial ☐
9. Case Record Form (CRF) ☐
10. Undertaking by Investigator(s) as per Appendix VII of Schedule Y and CV ☐
11. Undertaking by Sponsor(s) ☐
12. Prescribing information (of the drug circulated in other countries, if any) ☐

c. <u>For Phase III Clinical Trials</u>

1. Animal Pharmacology

g. Summary ☐

a. Data on specific pharmacological actions ☐

b. Data on general pharmacological actions

c. Data on follow-up and Supplemental Safety Pharmacology Studies ☐

d. Pharmacokinetics data ☐

2. Animal Toxicology ☐

   a. General Aspects

   b. Systemic Toxicity Studies

      i. Data of single dose toxicity studies ☐

      ii. Data of dose Ranging Studies ☐

      iii. Data of repeat-dose systemic toxicity studies ☐

   c. Data on Male Fertility Study ☐

   d. Data on Segment I (if female patients of child bearing age are going to be involved), and Segment III (for drugs to be given to pregnant or nursing mothers or where there are indications of possible adverse effects on foetal development) ☐

   e. Data on local toxicity with proposed route of clinical application (duration depending on proposed length of clinical exposure) ☐

   f. Data on allergenicity/Hypersensitivity (when there is a cause for concern or for parenteral drugs, including dermal application) ☐

   g. Data on photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential) ☐

   h. *Data on in vitro* genotoxicity ☐

3. Clinical study report of Phase I study ☐

4. Clinical study report of Phase II study ☐

5. The Proposed protocol for conducting the clinical trial ☐

6. Investigator's Brochure ☐

7. Patient Information Sheet and Informed Consent Form (ICF) as per Appendix V of Schedule Y ☐

8. Copy of 'Ethics Committee' approval letters (if available) ☐

9. Registration number of Ethics Committee/s that will oversee the trial ☐

10. Case Record Form (CRF) ☐

11. Undertaking by Investigator(s) as per Appendix VII of Schedule Y and CV ☐

12. Undertaking by Sponsor(s) ☐

13. Prescribing information (of the drug circulated in other countries, if any) ☐

14. Copy of proposed package insert ☐

d. <u>Phase IV Clinical Trials</u>

1. Animal Pharmacology

    e. Summary ☐

    a. Data on specific pharmacological actions ☐

    b. Data on general pharmacological actions

    c. Data on follow-up and Supplemental Safety Pharmacology Studies ☐

    d. Pharmacokinetics data ☐

2. Animal Toxicology ☐

    a. General Aspects

    b. Systemic Toxicity Studies ☐

        i. Data of single dose toxicity studies ☐

        ii. Data of dose Ranging Studies

        iii. Data of repeat-dose systemic toxicity studies ☐

    c. Data on Male Fertility Study

d. Data on Segment I (if female patients of child bearing age are going to be involved), and Segment III (for drugs to be given to pregnant or nursing mothers or where there are indications of possible adverse effects on foetal development) ☐ ☐

e. Data on local toxicity with proposed route of clinical application (duration depending on proposed length of clinical exposure) ☐ ☐

f. Data on allergenicity/Hypersensitivity (when there is a cause for concern or for parenteral drugs, including dermal application)

g. Data on photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential) ☐ ☐

h. *Data on in vitro* genotoxicity ☐

3. Clinical study report of Phase I study ☐

4. Clinical study report of Phase II study ☐

5. Clinical study report of Phase III study ☐

6. Approval from the licensing authority ☐

7. Copy of the approved drug label ☐

8. Pharmacovigilance plans and methods ☐

9. Investigator's Brochure ☐

10. Pharmacoepidemiological studies (if applicable) ☐

a. Protocol ☐

b. Patient Information Sheet and Informed Consent Form (ICF) as per Appendix V of Schedule Y (If applicable) ☐

c. Copy of 'Ethics Committee' approval letters (if available) ☐

d. Registration number of Ethics Committee/s that will oversee the trial ☐

e. Case Record Form (CRF) ☐

f. Undertaking by Investigator(s) as per Appendix VII of Schedule Y and CV ☐

g. Undertaking by Sponsor(s) ☐

e. <u>BA/BE studies</u>

1. Summary of the non clinical data ☐

2. Clinical data of Phase I studies ☐

3. Clinical data of Phase II studies ☐

4. Clinical data of Phase III studies ☐

5. The Proposed protocol for conducting the study ☐

6. Investigator's Brochure ☐

7. Patient Information Sheet and Informed Consent Form (ICF) as per Appendix V of Schedule Y ☐

8. Copy of 'Ethics Committee' approval letters (if available)

9. Registration number of Ethics Committee/s that will oversee the trial ☐

10. Case Record Form (CRF) ☐

11. Undertaking by Investigator(s) as per Appendix VII of Schedule Y and CV ☐

12. Undertaking by Sponsor(s) ☐

13. The Proposed protocol for conducting the clinical trial ☐

14. Investigator's Brochure ☐

15. Patient Information Sheet and Informed Consent Form (ICF) as per Appendix V of Schedule Y ☐

16. Copy of 'Ethics Committee' approval letters (if available) ☐

17. Registration number of Ethics Committee/s that will oversee the trial ☐

18. Case Record Form (CRF) ☐

19. Undertaking by Investigator(s) as per Appendix VII of Schedule Y and CV ☐

20. Undertaking by Sponsor(s) ☐

21. Copy of proposed Package Insert ☐

Consolidated List of 294 FDCs Licensed by SLAs

S.N.	Name of FDC	Category
1	5-bromosalicyl-4-chloranilide+Salicylic acid	Dermatologicals
2	Aceclofenac+Paracetamol+Chlorzoxazone	Orthopaedics
3	Aceclofenac+Paracetamol+Serratiopeptidase	Orthopaedics
4	Aceclofenac+Paracetamol+Tizanidine	Orthopaedics
5	Aceclofenac+Paracetamol+Tramadol	Orthopaedics
6	Aceclofenac+Serratiopeptidase	Orthopaedics
7	Aceclofenac+Tramadol	Orthopaedics
8	Acetaminophen+Codine phosphate	Cough&Cold
9	Acetyl salicylic acid+Ethoheptazine	Analgesics
10	Acetylcysteine+Selenomethionine+Choline Bitartrate+Pyridoxine+Folic Acid+Vitamin E+Cyanocobalamin+Chromium Nicotinate+Manganese Sulfate+Zinc Sulfate	Nutritionals
11	Acriflavine+Gentian violet+Brilliant green	Dermatologicals
12	Activated charcoal+Fungal distase+Lactic acid	GI
13	Adapalene+Methyl Paraben	Dermatologicals
14	Adenocyl Cobalamine+Carbonyl Ion+Folic Acid+Zinc Ascorbate	Nutritionals
15	Adenocynocobalamine+Carbonyl iron+Folic acid	Nutritionals
16	Alendronate sodium+Calcium Carbonate+Vit-D3	Orthopaedics
17	Alendronate sodium+Cholicalceferol+Calcium Citrate+Magnesium Hydroxide	Orthopaedics
18	Allantoin+Dimethicone+Methylparaben+Propylparaben	Dermatologicals
19	Allantoin+Triclosan+Vit-E+Zinc Oxide	Dermatologicals
20	Allantoin+Vit-E+Cammelina Sinensis	Dermatologicals
21	Allobarbitone+Phospho-dimethyl-isopropyl-pyrazolone	Analgesics
22	Aloe extract+allantocin+Alfa tocoferal acetate+D-panthemol+VitA	Dermatologicals
23	Aloe extract+Vit-E+Dimethicone+Glycerine	Dermatologicals
24	Aloe vera+Jojoba oil+Vit-E	Dermatologicals
25	Aloe vera+Orange oil	Dermatologicals
26	Aloe vera+Vit-e acetate	Dermatologicals
27	Aloe+tocopherol	Dermatologicals
28	Aloevera+Glycerine+PEG 100 stearate+Vit E	Dermatologicals
29	Aloevera+Jojoba oil+Wheat germ oil+Tea tree oil	Dermatologicals
30	Aloevera+Vit-E+Herbal	Dermatologicals
31	Alprazolam+Melatonin	CNS
32	Alprazolam+Propranolol	CNS
33	Amlodipine+Lovastatin	CVS
34	Amoxicillin+Cloxacillin+Lactic acid bacillus	Antimicrobial
35	Amoxicillin+Serratiopeptidase+Lactobacillus Sporogenes	Antimicrobial
36	Amoxycillin+Clavulanic acid+Lactic acid bacillus	Antimicrobial
37	Amoxycillin+Clavulanic Acid+Lactobacillus	Antimicrobial
38	Amoxycillin+Cloxacillin+Lactic acid bacillus	Antimicrobial
39	Amoxycillin+Cloxacillin+Lactic acid bacillus+Serrapeptase	Antimicrobial
40	Amoxycillin+Cloxacillin+Lacto Acid Bacillus	Antimicrobial
41	Amoxycillin+Lactic acid bacillus	Antimicrobial

42	Amoxycillin+Lactobacillus	Antimicrobial
43	Amoxycillin+Lactobacillus Acidophilus	Antimicrobial
44	Amoxycillin+Lactobacillus acidophilus+Clavulanic Acid	Antimicrobial
45	Amoxycillin+Lactobacillus acidophilus+Flucloxacillin Sodium	Antimicrobial
46	Amoxycillin+Serratiopeptidase	Antimicrobial
47	Ampicillin+Cloxacillin+Lactic acid bacillus	Antimicrobial
48	Ampicillin+Flucloxacillin Sodium Salt	Antimicrobial
49	Ampicillin+Flucloxacillin Sodium Salt+Lactobacillus Acidophilus	Antimicrobial
50	Ampicillin+Lactic acid bacillus	Antimicrobial
51	Analgin+Dextropopoxyphene	Analgesics
52	Analgin+Diazepam	Analgesics
53	Analgin+Diazepam+Diphenhydramine	CNS
54	Analgin+Diazepam+Paracetamol	Analgesics
55	Analgin+Diazepam+Propylene Glycol	Analgesics
56	Analgin+Dicyclomine+Diazepam	GI
57	Analgin+Dihydroethaverine chloride	GI
58	Analgin+Ketoprofen	Orthopaedics
59	Analgin+KET-P-PIPER.ETH -O-CARB M	Analgesics
60	Artesunate+Arteether+Artemether	Antimalarial
61	Atenolol+Hydrochlorothiazide+Amiloride	CVS
62	Atenolol+Losartan+Hydrochlorothiazide	CVS
63	Atorvastatin+Acetyl Salicylic acid	CVS
64	Atorvastatin+Acetyl Salicylic acid+Caffeine	Orthopaedics
65	Atorvastatin+Aspirin	CVS
66	Atorvastatin+Aspirin+Ramipril	CVS
67	Atorvastatin+Mecobalamine+Folic acid	CVS
68	Atorvastatin+Mecobalamine+Folic acid+Vit-B6	CVS
69	Atorvastatin+Omega 3 Fatty Acid	CVS
70	Atorvastatin+Ramipril	CVS
71	Atorvastatin+Ubidecarenone	CVS
72	Atorvastatin+Vitamin	CVS
73	Benfotimine+Pyridoxine+Mecobalamine+Inositol+Alphalipoic acid	Nutritionals
74	Calcium dobesilate+Decusate sodium	Antihaemorroid
75	Calcium dobesilate+Lignocaine	Antihaemorroid
76	Calcium dobesilate+Lignocaine+Hydrocortisone	Antihaemorroid
77	Calcium Dobesilate+Troxerutin	Antihaemorroid
78	Cefadroxyl+Ambroxol	Antimicrobial
79	Cefadroxyl+Lactic acid bacillus	Antimicrobial
80	Cefadroxyl+Probenecid	Antimicrobial
81	Cefdinir+Lactic acid bacillus	Antimicrobial
82	Cefixime+ambroxol+lactic acid	Antimicrobial
83	Cefixime+Ambroxol+Lactic acid bacillus	Antimicrobial
84	Cefixime+Lactic acid bacillus	Antimicrobial
85	Cefixime+Lactic acid bacillus+Ambroxol	Antimicrobial
86	Cefixime+Lactobacillus acidophilus	Antimicrobial
87	Cefixime+Lactobacillus acidophilus+Ambroxol	Antimicrobial
88	Cefixime+Lactobacillus Acvidophilus	Antimicrobial
89	Cefixime+Lactobacillus+Clavulanic Acid	Antimicrobial

90	Cefixime+Lactobacillus+Dicloxacillin	Antimicrobial
91	Cefixime+Ornidazole	GI
92	Cefpodoxime prozetil+Lactic acid bacillus	Antimicrobial
93	Cefpodoxime+Cloxacillin+Lactobacillus	Antimicrobial
94	Cefpodoxime+Lactic acid bacillus	Antimicrobial
95	Cefpodoxime+Lactobacillus	Antimicrobial
96	Cefprozil+Lactobacillus	Antimicrobial
97	Ceftriaxone+Vancomycin	Antimicrobial
98	Cefuroxime+Ornidazole	GI
99	Cefuroxime+Serratiopeptidase	Antimicrobial
100	Cepodoxime+Cloxacillin+Lactic acid bacillus	Antimicrobial
101	Chlormezanone+Paracetamol+Diclofenac sodium	Orthopaedics
102	Chlormezanone+Paracetamol+Ibuprofen	Orthopaedics
103	Chlorzoxazone+Ibuprofen+Paracetamol+Diclofenac+Oxyphenbutazone+Magnesium hydroxide	Orthopaedics
104	Chlorzoxazone+Nimesulide	Orthopaedics
105	Chlorzoxazone+Paracetamol	Orthopaedics
106	Chlorzoxazone+Paracetamol+Diclofenac	Orthopaedics
107	Chlorzoxazone+Paracetamol+Ibuprofen	Orthopaedics
108	Chlorzoxazone+Paracetamol+Ibuprofen+Diclofenac sodium	Orthopaedics
109	Chlorzoxazone+Paracetamol+Nimesulide	Orthopaedics
110	Ciprofloxacin+Tinidazole+Dicyclomine	GI
111	Clindamycin+Clotrimazole+Metronidazole	Antimicrobial
112	Clonidine+Chlorthalidone	CVS
113	Clonidine+Hydrochlorothiazide	CVS
114	Clopidogrel+Aspirin+Atorvastatin	CVS
115	Condroitin+Vitamin+Selenium zinc+Sulphate+Monohydrate	Nutritionals
116	Diclofenac potassium+Pitofenone hydrochloride+Fenpivireneum bromide + Paracetamol	Orthopaedics
117	Diclofenac potassium+Serratiopeptidase	Orthopaedics
118	Diclofenac Sodium+Rabeprazole	Orthopaedics
119	Diclofenac sodium+Serratiopeptidase	Orthopaedics
120	Diclofenac+Dextropropoxyphene+Paracetamol	Orthopaedics
121	Diclofenac+Famotidine	Orthopaedics
122	Diclofenac+Methyl Salicylate+Linoleic acid+Menthol	Orthopaedics
123	Diclofenac+Paracetamol+Chlormezanone	Orthopaedics
124	Diclofenac+paracetamol+Chlorzoxazone	Orthopaedics
125	Diclofenac+Paracetamol+Dextropropoxyphene	Orthopaedics
126	Diclofenac+Paracetamol+Serratiopeptidase	Orthopaedics
127	Diclofenac+paracetamol+Tizanidine	Orthopaedics
128	Diclofenac+Parcetamol+Chlorzoxazone	Orthopaedics
129	Diclofenac+Rabeprazole	Orthopaedics
130	Diclofenac+Serratiopeptidase	Orthopaedics
131	Diclofenac+Serratiopeptidase+Paracetamol	Orthopaedics
132	Diclofenac+Tizanidine	Orthopaedics
133	Diclofenace sodium+Serratiopepridase	Orthopaedics
134	Diclofenace+Serratiopeptidase	Orthopaedics
135	Dicyclomine+Dextromethorphan+Paracetamol	GI

136	Dicyclomine+Diclofenac Sodium+Paracetamol	GI
137	Dicyclomine+Mefenamic acid+Paracetamol	GI
138	Dicyclomine+Paracetamol+Analgin	GI
139	Dicyclomine+Paracetamol+Chlordiazepoxide	GI
140	Dicyclomine+Paracetamol+Clidinium Bromide	GI
141	Dicyclomine+Paracetamol+Clidinium bromide+Chlordiazepoxide	GI
142	Dicyclomine+Paracetamol+Dextropropoxyphene	GI
143	Dicyclomine+Paracetamol+Dextropropoxyphene+ Clordiazepoxide	GI
144	Dicyclomine+Paracetamol+Dimethylpolysiloxane	GI
145	Dicyclomine+Paracetamol+Phenylisopropyl Pyrazolon	GI
146	Dicyclomine+Paracetamol+Simethicone	GI
147	Dicyclomine+Ranitidine	GI
148	Dicyclomine+Serrartiopeptidase	Orthopaedics
149	Dicylomine+Parcetamol+Dimethylpolysiloxane	GI
150	Domperidone+Paracetamol	GI
151	Domperidone+Paracetamol+Tramadol	Analgesics
152	Domperidone+Ranitidine	GI
153	Doxycycline+Lactobacillus	Antimicrobial
154	Doxycycline+Tinidazole	GI
155	Drotaverine hydrochloride+Mefenamic Acid	GI
156	Drotaverine+Mefenamic acid	GI
157	Drotaverine+Nimesulide	GI
158	Drotaverine+Omeprazole	GI
159	Drotaverine+Paracetamol	GI
160	Duloxetine+Mecobalamin	CNS
161	Fenpiverinium bromide+Analgin+Pitofenone hydrochloride	GI
162	Fenpiverinium bromide+Diclofenac sodium+Pitofenone hydrochloride	GI
163	Fenpiverinium hydroxide bromide+Diclofenac sodium+Pitofenone hydrochloride	GI
164	Gabapentin+Mecobalamin+Thioctic acid	CNS
165	Gabapentin+Mecobalamin+Thioctic acid+Folic Acid+Pyridoxine	CNS
166	Gabapentin+Mecobalamine+Pyridoxine+Folic Acid	CNS
167	Gliclazide+Chromium picolinate	Antidiabetics
168	Glucosamine+Ascorbic Acid	Orthopaedics
169	Glucosamine+Boswellia Serrata	Orthopaedics
170	Glucosamine+Calcium Carbonate	Orthopaedics
171	Glucosamine+Cetylmyristate Oleate	Orthopaedics
172	Glucosamine+Chondroitin sulphate+Methyl sulphonyl methane	Orthopaedics
173	Glucosamine+Chondroitin sulphate+Vit+c+manganise sulphate	Orthopaedics
174	Glucosamine+Chondroitin+Vit C+Vit E+Manganese	Orthopaedics
175	Glucosamine+Chondroitin+Vit-C	Orthopaedics
176	Glucosamine+Chondroitin+Vit-C+Vit-E+Manganese	Orthopaedics
177	Glucosamine+Chondroitin+Vit-C+Vit-E+Manganese sulphate	Orthopaedics
178	Glucosamine+Chondroitin+Vit-C+Vit-E+Manganese sulphate+Sodium borate+Selenium dioxide	Orthopaedics
179	Glucosamine+Colecalciferol+Manganese+Ascorbic acid	Orthopaedics
180	Glucosamine+Manganese	Orthopaedics
181	Glucosamine+Mecobalamin+Dimethyl Sulfone	Orthopaedics

182	Glucosamine+Mecobalamine	Orthopaedics
183	Glucosamine+Mecobalamine+Milk calcium	Orthopaedics
184	Glucosamine+Methyl sulphonyl methane	Orthopaedics
185	Glucosamine+Methylsulfonal Methenamine+Cetylmyristate	Orthopaedics
186	Glucosamine+Vit C+Calcium+Methyl Sulfonyl Methane+Chondroitin+Manganese	Orthopaedics
187	Glucosamine+Vit-C+Vit-E+Chondroitin sulphate+Methyl sulfonyl methane+Manganese sulphate	Orthopaedics
188	Gluosamine sulphate+Chondroitin+sulphate+Vit-E+Manganese	Orthopaedics
189	Gluosamine+Calcium+Vit-D3	Orthopaedics
190	Hydrochlorothiazide+Ramipril+Losartan Potassium Salt	CVS
191	Ibuprofen+Carisoprodol	Orthopaedics
192	Ibuprofen+Codeine	Orthopaedics
193	Ibuprofen+Colchicine	Orthopaedics
194	Ibuprofen+Dextropropoxyphene	Orthopaedics
195	Ibuprofen+Dextropropoxyphene+Paracetamol	Orthopaedics
196	Ibuprofen+Paracetamol+Caffeine	Cough&Cold
197	Ibuprofen+Paracetamol+Colchicine	Orthopaedics
198	Ibuprofen+Paracetamol+Dextropropoxyphene	Orthopaedics
199	Ibuprofen+paracetamol+magnesium triscillicate	Orthopaedics
200	Ibuprofen+Paracetamol+Magnesium trisilicate	Orthopaedics
201	Ibuprofen+Paracetamol+Oxyphenbutazone+Phenylisopropyl pyrazolon	Orthopaedics
202	Ibuprofen+Paracetamol+Phenylepherine+Chlorpheniramine maleate	Cough&Cold
203	Ibuprofen+Paracetamol+Serratiopeptidase	Orthopaedics
204	Ibuprofen+Pseudoephedrine+Chlorpheniramine maleate	Cough&Cold
205	Ibuprofen+Tizanidine	Orthopaedics
206	Lansoprazole+Amoxycillin+Clarithromycin	GI
207	Lansoprazole+Amoxycillin+Tinidazole	GI
208	Lansoprazole+Domperidone	GI
209	Lansoprazole+Tinidazole+Clarithromycin	GI
210	Levocetrizine+Montelukast	Antihistamines
211	Levofloxacin+Ambroxol	Antimicrobial
212	Levofloxacin+Ornidazole	GI
213	Lincomycin+Lactobacillus	Antimicrobial
214	Losartan+Hydrochlorothiazide+Atenolol	CVS
215	Losartan+Hydrochlorothiazide+Ramipril	CVS
216	Losartan+Perindopril	CVS
217	Mebeverine+Alprazolam	GI
218	Mebeverine+Plantago Ovata	GI
219	Mecobalaminalphalipoic acid+Folic acid+Vit-b6+Choline	Nutritionals
220	Mecobalamine+Alpha lipoic acid	Nutritionals
221	Mecobalamine+Alphalipoic acid+Folic acid	Nutritionals
222	Mecobalamine+Alphalipoic acit+Vit-b1+Folic acid	Nutritionals
223	Mecobalamine+Biotin	Nutritionals
224	Mecobalamine+Calcium Pantothenate	Nutritionals
225	Mecobalamine+Carotinoid+Alpha lipoic acid+Chromim+Vit-b1+Vit-b complex	Nutritionals
226	Mecobalamine+Folic acid	Nutritionals

227	Mecobalamine+Methenamine mandelate	Nutritionals
228	Mecobalamine+Vit-A+Vit-E+Vit-C+Vit-B1+Vit-B6+Vit-D3+Selenium	Nutritionals
229	Mecobalamine+Vitamins+Minerals	Nutritionals
230	Mecobalamine+Vit-b1+Vit-b2+Vit-b6+Folic acid	Nutritionals
231	Mecobalamine+Vit-B1+Vit-B6+Folic acid+Alpha lipoic acid	Nutritionals
232	Mecobalamine+Vit-b1+Vit-b6+Nicotinamide+D-panthenol	Nutritionals
233	Mecobalamine+Vit-B6+Folic acid	Nutritionals
234	Mefenamic acid+Dicyclomine	GI
235	Meloxicam+Paracetamol	Orthopaedics
236	Metformin hydrochloride+Mecobalamine	Antidiabetics
237	Methocarbamol+Ibuprofen	Orthopaedics
238	Methocarbamol+Nimesulide	Orthopaedics
239	Methocarbamol+Paracetamol	Orthopaedics
240	Metoclopramide hydrochloride+Paracetamol	GI
241	Mupirocin+Metronidazole	Dermatologicals
242	Naproxen+Domperidone	Orthopaedics
243	Nimesulide+Paracetamol+Chlorzoxazone	Orthopaedics
244	Nimesulide+Paracetamol+Serratiopeptidase	Orthopaedics
245	Nimesulide+Phenylpherine+Chlorphenrimane maleate+Caffeine	Cough&Cold
246	Nimesulide+P-Piperidinoethoxy-O-Carbomethoxybenzophenone+Diphenyl Piperidenoethyl Acetamide Bromomethylate	GI
247	Nimesulide+pseudoephedrine+Cetirazine	Cough&Cold
248	Norfloxacin+Ornidazole	GI
249	Norfloxacin+Tinidazole+Dicyclomine	GI
250	Norfloxacin+Tinidazole+Lactobacillus	GI
251	Norfloxacin+Tinidazole+Loperamide	GI
252	Ofloxacin+Diclofenac+Lignocaine	Orthopaedics
253	Ofloxacin+Lactic acid bacillus	Antimicrobial
254	Ofloxacin+Metronidazole	GI
255	Ofloxacin+Ornidazole+Lactobacillus	GI
256	Ofloxacin+Prednisolone	Orthopaedics
257	Ofloxacin+Tinidazole	GI
258	Ondansetron+Omeprazole	GI
259	Ondansetron+Paracetamol	GI
260	Ondansetron+Ranitidine	GI
261	Ornidazole+Doxycycline	GI
262	Ornidazole+Flucanazole+Azithromycin	Antimicrobial
263	Paracetamol+Alprazolam	Analgesics
264	Paracetamol+Analgin	Analgesics
265	Paracetamol+Diclofenac Sodium+Amoxicillin+Cloxacillin+Pantoprazole+Lactic Acid Bacillus+Serrapeptase	Analgesics
266	Paracetamol+Diclofenac sodium+Magnesium Trisilicate+Chlorphenamine Maleate	Orthopaedics
267	Paracetamol+Diclofenac+Chlorzoxazone	Orthopaedics
268	Paracetamol+Dicycloverine+Mefenamic	GI
269	Paracetamol+Ketoprofen+Dextropropoxyphene	Orthopaedics
270	Paracetamol+Lignocaine	Analgesics
271	Pregabalin+Mecobalamine	CNS

272	Pregabalin+Mecobalamine+Pyridoxine+Thioctic Acid+Folic Acid	CNS
273	Pregabalin+Thioctic Acid+Folic Acid+Pyridoxine	CNS
274	Propranolol+Alprazolam	CVS
275	Propranolol+Diazepam	CVS
276	Propranolol+Hydrallazine	CVS
277	Propranololol+Hydrochlorothiazide+Dihydrallazine	CVS
278	Ranitidine+Cisapride	GI
279	Ranitidine+Dicyclomine	GI
280	Ranitidine+Dicyclomine+Clidinium bromide	GI
281	Ranitidine+Dicyclomine+Nimesulide	GI
282	Ranitidine+Dicycloverine+Simethicone	GI
283	Ranitidine+Domperidone	GI
284	Ranitidine+Drotaverine	GI
285	Ranitidine+Omeprazole	GI
286	Ranitidine+Ondansetron	GI
287	Roxithromycin+Ambroxol	Antimicrobial
288	Roxithromycin+Carbocisteine	Antimicrobial
289	Satranidazole+Ofloxacin	GI
290	Telmisartan+Ramipril+Hydrochlorthiazide	CVS
291	Tizanidine+Diclofenac sodium+Paracetamol	Orthopaedics
292	Tizanidine+Nimesulide+Paracetamol	Orthopaedics
293	Torsemide+Spironolactone	CVS
294	Tramadol+Paracetamol+Domperidone	Analgesics