

Revised checklist for BA/BE NOC effective from 01st February 2014
(Draft for comments before 25 Jan 14)

**Documents to be submitted for grant of permission to conduct
BA/BE studies in Human Subjects/Patients for export purpose.**

The office of Drugs Controller General (India) at CDSCO (HQ) FDA Bhavan, New Delhi has been reviewing applications on behalf of Pharmaceutical companies, both Manufacturers and Importers as well as CRO's, requesting for the approval to carry out BE studies with various pharmaceutical dosage formulations on Indian subjects. The office of DCG(I) would like to ensure the demonstration of the safety and efficacy of generics against corresponding innovator drugs; to ensure they are comparable and safe for consumption by human subjects. An Assessment of "interchangeability" between the generic and the innovator product is carried out by a study of "in vivo equivalence" or "bioequivalence" (BE). In view of the above, the office of DCGI would like to ensure the uniformity of documents to be submitted to the Directorate for review and approval of BE-NOC's to meet tenets of Schedule Y of Drugs and Cosmetics Act 1940 & Rules 1945 and also Indian Good Clinical Practices (GCP).

All BE-NOC applications should be accompanied with the following documents consisting of proper index with page numbers in legible form.

Requirements for conducting BE study of a new molecule not approved in India but approved by other countries.

1. Application in Form-44 duly signed, by the Authorized signatory with details of name and designation.
2. Treasury Challan (TR – 6) of ` 25000/- as per Drugs & Cosmetic Rules (Medical and Public Health Account: 0210).
3. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per appendix VII of Schedule "Y" of Drugs and Cosmetic Rules.
4. BA/BE Centre approval copy issued by DCG(I), New Delhi, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.
5. Sponsor's Authorization letter duly signed by the Authorized Signatory on company letterhead.
6. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio-visual recording system as per

Schedule Y guidelines; & copy of approval of protocol from the IEC, if available.

7. Copy of registration of Independent/Institutional Ethics Committee (IEC) under Rule-122DD from the Office of Drugs Controller General (India), New Delhi.
8. The study synopsis.
9. Undertaking letter from the sponsor stating that you will provide complete medical care as well as compensation for the injury or Death and statement to this effect should be incorporated in the Informed Consent Form further in case of such injuries or Deaths the details of compensation provided should be intimated to this Directorate as per Rule 122 DAB of D&C Act 1940 & Rules there under.
10. Non-clinical and clinical data as per Appendix I of Schedule Y.
11. Published reports of Pharmacokinetic and Pharmacodynamics studies carried out in healthy subjects/patients demonstrating safety and tolerability of the molecule.
12. Regulatory approval status of the drug indicating the strength, dosage form and countries.
13. Names of the countries where the drug is currently being marketed (to be mentioned in the covering letter also).
14. Package insert/ prescribing information of the product.
15. Chemical and Pharmaceutical data including stability data.
16. Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case Oral Solid dosage forms.
17. For multiple dose BE study adequate supporting safety data and PK/PD should be submitted covering the duration of period for which the study has to be conducted.
18. For all Injectable, the sub-acute toxicity should be submitted on the Test product of the sponsor, studied in at least two species for minimum 14 days. If Regulatory Guidance is available provide a copy of the same.
19. For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Healthy Human subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted. If regulatory guidance is available provide a copy of the same.
20. For conducting BE studies with reference to cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Patients a Scientific justification with special emphasis on Safety with a proper Risk Mitigation Strategy should be submitted.
21. Report of any study related deaths during last 3 years.

22. Address details of the IEC Location and study site location.

New drugs approved in India within period of one year:-

1. Application in Form-44 duly signed, by the Authorized signatory with details of name and designation.
2. Treasury Challan (TR – 6) of ` 25000/- as per Drugs & Cosmetic Rules (Medical and Public Health Account: 0210).
3. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per appendix VII of Schedule “Y” of Drugs and Cosmetic Rules.
4. Regulatory status of the Drug in India.
5. BA/BE Centre approval copy issued by DCG(I), New Delhi, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.
6. Sponsor’s Authorization letter duly signed by the Authorized Signatory on company letterhead.
7. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio-visual recording system as per Schedule Y guidelines; & copy of approval of protocol from the IEC, if available.
8. Copy of registration of Independent/Institutional Ethics Committee (IEC) under Rule-122DD from the Office of Drugs Controller General (India), New Delhi.
9. The study synopsis.
10. Undertaking letter from the sponsor stating that you will provide complete medical care as well as compensation for the injury or Death and statement to this effect should be incorporated in the Informed Consent Form further in case of such injuries or Deaths the details of compensation provided should be intimated to this Directorate as per Rule 122 DAB of D&C Act 1940 & Rules there under.
11. Published reports of Pharmacokinetic and Pharmacodynamics studies carried out in healthy subjects/ patients demonstrating safety and tolerability of the molecule.
12. Package insert/ prescribing information of the product.
13. Chemical and Pharmaceutical data including stability data.
14. Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case Oral Solid dosage forms.
15. For Multiple dose BE study adequate supporting safety data & PK/PD data should be submitted covering the duration of period for which the

study has to be conducted. If Regulatory Guidance is available provide a copy of the same

16. For all Injectable, the sub-acute toxicity should be submitted on the Test product of the sponsor, studied in at least two species for minimum 14 days.
17. For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Healthy Human subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted.
18. For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Patients a Scientific justification with special emphasis on Safety with a proper Risk Mitigation Strategy should be submitted. If regulatory guidance is available provide the copy of the same.
19. Report of any study related deaths during last 3 years.
20. Address details of the IEC Location and study site location.

New Drugs approved within period of more than 1 year & less than 4 years:-

1. Application in Form-44 duly signed, by the Authorized signatory with details of name and designation.
2. Treasury Challan (TR – 6) of ` 15000/- as per Drugs & Cosmetic Rules (Medical and Public Health Account: 0210).
3. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per appendix VII of Schedule “Y” of Drugs and Cosmetic Rules.
4. Regulatory status of the Drug in India.
5. BA/BE Centre approval copy issued by DCG(I), New Delhi, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.
6. Sponsor’s Authorization letter duly signed by the Authorized Signatory on company letterhead.
7. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio-visual recording system as per Schedule Y guidelines; & copy of approval of protocol from the IEC, if available.
8. Copy of registration of Independent/Institutional Ethics Committee (IEC) under Rule-122DD from the Office of Drugs Controller General (India), New Delhi.
9. The study synopsis.

- 10.Undertaking letter from the sponsor stating that you will provide complete medical care as well as compensation for the injury or Death and statement to this effect should be incorporated in the Informed Consent Form further in case of such injuries or Deaths the details of compensation provided should be intimated to this Directorate as per Rule 122 DAB of D&C Act 1940 & Rules there under.
- 11.Chemical and Pharmaceutical data including stability data.
- 12.Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case Oral Solid dosage forms.
- 13.For Multiple dose BE study adequate supporting safety data (PK/PD) should be submitted covering the duration of period for which the study has to be conducted. If Regulatory Guidance is available provide a copy of the same
- 14.For all Injectables, the sub-acute toxicity should be submitted on the Test product of the sponsor, studied in at least two species for minimum 14 days.
- 15.For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Healthy Human subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted.
- 16.For conducting BE studies with reference to cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Patients a Scientific justification with special emphasis on Safety with a proper Risk Mitigation Strategy should be submitted.
- 17.Report of any study related deaths during last 3 years.
- 18.Address details of the IEC Location and study site location.

BE NOC for all the drug products in modified release form irrespective of their approval status:-

1. Application in Form-44 duly signed, by the Authorized signatory with details of name and designation.
2. Treasury Challan (TR – 6) of ` 15000/- as per Drugs & Cosmetic Rules (Medical and Public Health Account: 0210) for approved in India or if not approved in India TR- 6 of Rs. 25000/-.
3. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per appendix VII of Schedule “Y” of Drugs and Cosmetic Rules.
4. Regulatory status of the Drug in India.

5. BA/BE Centre approval copy issued by DCG(I), New Delhi, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.
6. Sponsor's Authorization letter duly signed by the Authorized Signatory on company letterhead.
7. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio-visual recording system as per Schedule Y guidelines; & copy of approval of protocol from the IEC, if available.
8. Copy of registration of Independent/Institutional Ethics Committee (IEC) under Rule-122DD from the Office of Drugs Controller General (India), New Delhi.
9. The study synopsis
- 10.Undertaking letter from the sponsor stating that you will provide complete medical care as well as compensation for the injury or Death and statement to this effect should be incorporated in the Informed Consent Form further in case of such injuries or Deaths the details of compensation provided should be intimated to this Directorate as per Rule 122 DAB of D&C Act 1940 & Rules there under.
- 11.Chemical and Pharmaceutical data including stability data.
- 12.Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case Oral Solid dosage forms.
- 13.For Multiple dose BE study adequate supporting safety data & PK/PD data should be submitted covering the duration of period for which the study has to be conducted. If Regulatory Guidance is available provide a copy of the same.
- 14.For all Injectable, the sub-acute toxicity should be submitted on the Test product of the sponsor, studied in at least two species for minimum 14 days.
- 15.For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Healthy Human subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted.
- 16.For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Patients a Scientific justification with special emphasis on Safety with a proper Risk Mitigation Strategy should be submitted.
- 17.Report of any study related deaths during last 3 years.
- 18.Address details of the IEC Location and study site location.

Application for BE NOC for Export of old drug (Drugs approved more than 4 years) except modified release dosage form:-

1. Covering letter of the firm.
2. Regulatory status of the Drug in India indicating dosage form & strength.
3. Form-12 application along with relevant Treasury Challan (cdsco.nic.in).
4. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per appendix VII of Schedule "Y" of Drugs and Cosmetic Rules.
5. BA/BE Centre approval copy issued by DCG(I), New Delhi, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.
6. Sponsor's Authorization letter duly signed by the Authorized Signatory on company letterhead.
7. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio-visual recording system as per Schedule Y guidelines; & copy of approval of protocol from the IEC, if available.
8. Copy of registration of Independent/Institutional Ethics Committee (IEC) under Rule-122DD from the Office of Drugs Controller General (India), New Delhi.
9. The study synopsis
- 10.Undertaking letter from the sponsor stating that you will provide complete medical care as well as compensation for the injury or Death and statement to this effect should be incorporated in the Informed Consent Form further in case of such injuries or Deaths the details of compensation provided should be intimated to this Directorate as per Rule 122 DAB of D&C Act 1940 & Rules there under.
11. Pharmaceutical data including stability data.
12. Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case Oral Solid dosage forms.
13. For Multiple dose BE study adequate supporting safety data & PK/PD data should be submitted covering the duration of period for which the study has to be conducted. If Regulatory Guidance is available provide a copy of the same.
14. For all Injectable, the sub-acute toxicity should be submitted on the Test product of the sponsor, studied in at least two species for minimum 14 days.
15. For conducting BE studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc in Healthy Human

subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted.

16. For conducting BE studies with reference to cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances etc. in Patients a Scientific justification with special emphasis on Safety with a proper Risk Mitigation Strategy should be submitted.

17. Report of any study related deaths during last 3 years.

18. Address details of the IEC Location and study site location.

All above requirements are general in nature, however depending on the nature of the drug, disease and studies further specific information may also be required to be furnished by the firm.

NOTE: For all Un-approved Drugs, Drugs less than 1 year old, Modified Release Formulations for which the Directorate has issued BE-NOC's, all BA/ BE centres are hereby requested to furnish an annual status report of the Project Details, the Start and End date of the Project, Location of the Study, SAE's encountered, Study outcome etc to the Directorate for its review and record purpose on or before 15th January of the following year to ensure the safety and wellbeing of the participating healthy human subjects/patients.

(Dr. A. Ramkishan)
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