Genentech Inc and Others Vs. Drugs Controller General of India

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Court : Delhi

Decided On : Apr-25-2016

Judge : Manmohan Singh

Appeal No. : I.A.No. 23041 of 2015 & I.A.No. 25289 of 2015 in CS(OS) No. 3284 of 2015

Appellant : Genentech Inc and Others

Respondent : Drugs Controller General of India

Judgement :

Manmohan Singh, J.

1. The plaintiffs filed the present suit for injunction seeking various prayers inter alia decree a decree of declaration that the defendant's drug has not been tested as a biosimilar product under applicable law, defendant No. 3's CTR Registration Number CTR/2013/04/ 003549 is invalid and is not in accordance with applicable law. A decree of declaration that the approval granted by defendant No. 1 on October 29, 2012 to defendant No. 3's clinical trial protocol for the defendant's Drug is invalid and is not in accordance with applicable law and the manufacturing and marketing authorisation approved on 2nd June, 2015 by defendant No. 1 to defendant No. 3 for the defendant's drug for all of the Indications is invalid.

2. By this order I propose to decide the above mentioned two applications.

3. It is alleged in the plaint that the suit has been filed on account of the imminent threat and credible apprehension of the launch of defendant No. 3's drug, TrastuRel ("TrastuRel"), a purported biosimilar version of the plaintiffs' biological drug Trastuzumab (the "plaintiffs' Trastuzumab") for the treatment of HER2+ metastatic breast cancer, HER2+ early breast cancer and HER2+ metastatic gastric cancer (collectively, "Indications"). The main contention in the suit is that the defendant No. 3 for their product namely TrastuRel has not been adequately tested for HER2+ metastatic breast cancer in accordance with the applicable law in India, i.e. the Drugs and Cosmetics Act, 1940, as amended (the "Drugs Act"), the Drugs and Cosmetics Rules, 1945, as amended (the "Drugs Rules"), the Guidelines on Similar Biologies, 2012 (the "Biosimilar Guidelines") and other applicable law for the purpose of obtaining appropriate approvals, or tested at all for HER2+ early breast cancer and HER2+ metastatic gastric cancer (the "Additional Indications"). The averments and facts made in the injunction application and plaint are common, thus the plaint is being dealt with.

4. The injunction is sought by the plaintiffs restraining defendant No. 3 from launching, introducing, selling, marketing and/or distributing the defendant's drug in the Indian market as 'Trastuzumab' or otherwise for any of the Indications, pursuant to the marketing authorisation to be granted by defendant No. 1, without appropriate tests having been conducted on the defendant's drug under the Drugs Act, the Drugs Rules and Biosimilar Guidelines and from representing the defendant's drug as 'Trastuzumab'.

5. Plaintiff No. 1, Genentech Inc., a corporation incorporated in the State of Delaware, USA, with its principal office at 1DNA Way, South San Francisco, Cahfomia 94080, USA, is an affiliate of plaintiff No. 3. Plaintiff No. 1 claims to be the innovator of the biological drug Trastuzumab. It is also the registered proprietor of the trademark HERCEPTIN. worldwide (including India). Plaintiff No. 1 obtained registration of the mark HERCEPTIN in India under Class 5 - Registration No. 358259 dated April 23, 2005 valid up to October 9, 2018. Plaintiff No. 1 was granted a secondary, formulation patent in relation to Trastuzumab from the Controller General of Patents, Designs and Trademarks of India, which was deemed to be effective from May 3, 1999 and which lapsed on May 3, 2013.

Plaintiff No.2, Roche Products (India) Private Limited, a company incorporated under the Companies Act, 1956, as amended (the "Companies Act"), with its registered office at 1503, 15th Floor, The Capital, Bandra Kurla Complex, Bandra (East), Mumbai - 400 051, is an affiliate of plaintiff No. 3, and is the importer and marketer of innovator molecule Trastuzumab in India. In India, the plaintiffs' Trastuzumab is sold under the brand names HERCEPTIN., HERCLON and BICELTIS. The plaintiffs' Trastuzumab is an accepted treatment for certain forms of cancer on a worldwide basis and enjoys a global reputation.

Plaintiff No. 3, F. Hoffmann-La Roche AG, a joint stock company incorporated under the laws of Switzerland, with its headquarters at Grenzacherstrasse 124, CH-4070 Basel, Switzerland, is an affiliate of plaintiffs No. 1 and 2, and the manufacturer of innovator molecule Trastuzumab. Plaintiffs No. 1, 2 and 3 are hereinafter collectively referred to as the "plaintiffs".

5.1 defendant No. 1, the Drug Controller General of India, Central Drugs Standard Control Organisation, Ministry of Health and Family Welfare, Government of India, is responsible for the approval of new drugs in India.

The defendant No. 2, Department of Biotechnology, under the Ministry of Science and Technology, was, inter alia, responsible for drafting and introducing the Biosimilar Guidelines after consultation with several stakeholders and for granting various approvals for biologic drugs in India, including approval for import of cell lines and approval for conducting pre-clinical trials, evaluating pre-clinical trial reports and recommending the conduct of the various phases of clinical trials.

Defendant No. 3, Reliance Life Sciences Private Limited, is a company registered under the Companies Act, 1956, as amended, with its registered office at Dhirubhai Ambani Life Sciences Centre R-282, 15 TTC Area of MIDC, Thane Belapur Road, Rabale, Navi Mumbai - 400701. Defendant No. 3 has been registered with the Clinical Trials Registry - India (the "CTRI") as the sponsor of clinical trials of a purported biosimilar version of the plaintiffs' Trastuzumab (i.e., the defendant's drug).

Brief Facts as per Plaint are:-

6. The plaintiffs are globally engaged in the business of health care in the fields of pharmaceuticals and diagnostics. In 1990, plaintiff No. 1 developed a biological drug containing the active ingredient Trastuzumab, a humanised monoclonal antibody. The plaintiffs' Trastuzumab is produced by Chinese hamster ovary (CHO) cells, in which the DNA coding for human preproinsulin and for the humanised immunoglobulin chains along with two selectable markers have been inserted. The Plaintiffs' Trastuzumab produced by these cells is thus a humanised antibody with both murine and human components from the Chinese Hamster Ovary cell. The plaintiffs' Trastuzumab binds specifically to the human epidermal growth factor receptor 2 (''HER2'') protein and is designed to target and block HER2 protein over expression. In addition to blocking HER2 protein over expression, the plaintiffs' Trastuzumab also triggers an immune response in the body to destroy the particular cell it attach itself to. The plaintiffs' Trastuzumab has a two-fold role in containing and curing certain forms of cancer.

6.1 Between 1992 and 1998, extensive global clinical trials (Phase I, Phase II and Phase III) were carried out by plaintiff No. 1 to test the safety, efficacy and quality of Trastuzumab for the indication, HER 2+ metastatic breast cancer and the plaintiffs' Trastuzumab received manufacturing and marketing approvals worldwide after rigorous tests to confirm its safety, efficacy and quality. Among other approvals, the plaintiffs' Trastuzumab was approved by the U.S. Food and Drug Administration in September 1998 for HER 2+ metastatic breast cancer and by the European Medicines Agency in August 2000 for HER 2+ metastatic breast cancer. This biological drug has been sold by the plaintiffs worldwide since 1998, inter alia, under the well-known trademark HERCEPTIN. The plaintiffs were the first to introduce a targeted biological treatment for the patients of HER2+ metastatic breast cancer with the launch of HERCEPTIN. in 1998. Thereafter, HERCEPTIN. has been globally approved for the treatment of HER 2+ early breast cancer and HER 2+ metastatic gastric cancer. HERCEPTIN. has a well-established and documented track record of quality, safety and efficacy and has become the accepted treatment for the above referenced forms of cancer on a worldwide basis and enjoys a global reputation.

6.2. In India, the plaintiffs' Trastuzumab has been marketed under the brand name HERCEPTIN. for more than 12 years. HERCEPTIN. is prescribed as a targeted therapy for the treatment of the above referenced forms of cancer even in India. HERCEPTIN. is one of the brands under which the plaintiffs' Trastuzumab has been marketed in India. Until August 2012, the plaintiffs' Trastuzumab was promoted by the plaintiffs in India under the brand name HERCEPTIN.. The medical community associates the innovator molecule 'Trastuzumab' with the plaintiffs and with plaintiff No. 1's trademark HERCEPTIN. The brand 'HERCEPTIN.' has acquired extensive goodwill and a distinctive reputation.

6.3 HERCEPTIN is the brand which is most commonly associated with 'Trastuzumab' worldwide including in the Indian market. The plaintiffs also import and market the plaintiffs' Trastuzumab in India under the brand name HERCLONTM. Further, under a brand user agreement with plaintiff No. 3, Emcure Pharmaceuticals Limited distributes the plaintiffs' Trastuzumab in India under the brand name BICELTIS. Plaintiff No. 1is the registered proprietor of BICELTIS. in India (under Class 5 - Registration No. 945910 dated February 22, 2011 valid up to April 23, 2019).

6.4 The plaintiffs obtained approval for the import and marketing of the plaintiffs' Trastuzumab in India for the treatment of HER 2+ metastatic breast cancer in the year 2002. Such approval was granted by defendant No. 1 on October 11, 2002 under Rule 122A of the Drugs Rules. The plaintiffs' Trastuzumab is presently imported into India by plaintiff No. 2.

6.5. Thereafter, approvals under Rule 122A of the Drugs Rules were granted by defendant No. 1 for the import and marketing of the plaintiffs' Trastuzumab in India for the treatment of HER 2+ early breast cancer and HER 2+ metastatic gastric cancer on August 7, 2006 and April 13, 2010 respectively based on the above referenced global clinical trials.

6.6. Defendants No. 1 and 2 framed the Biosimilar Guidelines which came into effect on September 15, 2012, in order to provide a legal framework for evaluation and approval of biosimilar drugs in India. The Biosimilar Guidelines have introduced a regime for comparative testing between a purported biosimilar drug

and the innovator biological drug. The Biosimilar Guidelines were released publicly at the Biotechnology Industry Association conference in Boston in June, 2012 to show India's compliance with international practices and the applicable regime of the World Health Organisation. At this conference, defendants No. 1 and 2 made public statements indicating that they will implement and follow the Biosimilar Guidelines in India.

6.7 Upon becoming aware of defendant No. 3's recent endeavour to seek approval for the defendant's drug as a biosimilar version of the plaintiffs' Trastuzumab, the plaintiffs made enquiries, searched for information from the CTRI website, and after a review of information made publicly available by defendant No. 1, have become aware that the defendant's drug fails to full fill the safety criteria mandated by the Drugs Rules or the Biosimilar Guidelines. The defendants have failed to demonstrate the biosimilarity of the defendant's drug with the plaintiffs' Trastuzumab in compliance with the Drugs Act and Drugs Rules, as also the Biosimilar Guidelines. The defendant's drug is not a biosimilar drug with the plaintiffs' Trastuzumab.

7. It is averred in the plaint that after the issuance of the Biosimilar Guidelines, all applications for manufacturing and marketing authorisation of similar biologies in India are required to be evaluated on the basis of the standards set forth in the Biosimilar Guidelines read with the Drugs Act and the Drugs Rules. The Drugs Act, the Drugs Rules and the Biosimilar Guidelines ensure that adequate tests are conducted prior to the approval of biosimilars and it is essential that they are followed at all stages of product development, testing and approval of a purported biosimilar drug to ensure the safety of patients. A thorough consideration should be given to the scientific basis of the study design, objectives, study end points, sample size and study duration of the applicant's product before approval is granted to a biosimilar drug and only products which have been approved under the Biosimilar Guidelines read with the Drugs Act and the Drugs Rules should be allowed to be represented as biosimilar products.

8. It is mentioned in the plaint that the approval of the defendant's CTR by defendant No. 1 on October 29, 2012; (ii) the clinical trials purportedly conducted

by defendant No. 3 pursuant to the defendant's CTR; and (iii) the Subject Expert Committee (SEC) Recommendation relating to the grant of a marketing authorisation to the defendant's drug for the Additional Indications are in violation of the Drugs Act, the Drugs Rules and the Biosimilar Guidelines. Defendant No. 3 has failed to establish biosimilarity between the Defendant's Drug and the plaintiffs' Trastuzumab on the basis of the clinical trials purportedly conducted pursuant to the Defendant's CTR. Consequently, the impending marketing authorisation on the basis of the defendant's CTR and SEC Recommendation for the defendant's Drug from defendant No. 1 will be in violation of the Drugs Act, the Drugs Rules and the Biosimilar Guidelines and deserves to be restrained by this Court.

8.1 The SEC Recommendation, granted on the basis of alleged comparability of the defendant's drug with the plaintiffs' Trastuzumab, reflects that defendant No. 3 has misrepresented the defendant's Drug as similar and/or comparable to the plaintiffs Trastuzumab/ HERCEPTIN. As stated above, the defendant's CTR is not in compliance with the Drugs Act, the Drugs Rules and the Biosimilar Guidelines. Defendant No. 3 has failed to establish comparability or biosimilarity between the defendant's drug and the plaintiffs' Trastuzumab on the basis of tests purportedly conducted pursuant to the defendant's CTR and the defendant's drug is not biosimilar to the plaintiffs' Trastuzumab.

8.2 There may be misrepresentations to deceive the doctors and patients using 'Trastuzumab' for the treatment of HER 2+ metastatic breast cancer, HER 2+ early breast cancer and HER 2+ metastatic gastric cancer regarding the therapeutic benefit, quality, efficacy and safety of the defendant's drug. Defendant No. 3, through such misrepresentations, will also take unfair advantage of the reputation and goodwill enjoyed by the plaintiffs in relation to the plaintiffs' Trastuzumab and the brand names HERCEPTIN., HERCLON. and BICELITIS.

8.3 The defendant No. 3 is trying to appropriate the business reputation of the plaintiffs in relation to the plaintiffs' Trastuzumab. The plaintiffs' Trastuzumab is the accepted treatment for certain forms of cancer on a worldwide basis and enjoys a global reputation. It is for this reason alone that defendant No. 3 seeks to

manufacture a biosimilar version of the plaintiffs' Trastuzumab in India. However, defendant No. 3 has not produced a biosimilar version of the plaintiffs' Trastuzumab and simply seeks to appropriate the reputation of the plaintiffs and the plaintiffs' Trastuzumab for their commercial advantage.

8.4 Defendant No. 3 has not undertaken requisite clinical trials and has not generated adequate data to establish, inter alia, the safety, efficacy and immunogenicity of the defendant's drug. The clinical trials purportedly conducted by defendant No. 3 pursuant to the defendant's CTR are not in accordance with applicable law and are inadequate to establish comparability between the defendant's drug and the plaintiffs' Trastuzumab.

8.5 The defendant No. 3 might have reproduced data relating to the plaintiffs' Trastuzumab, including data relating to the Additional Indications, in the package insert for the defendant's drug and fraudulently present this data as data for the defendant's drug itself, without appropriate tests having been conducted on the defendant's drug under the Drugs Act, the Drugs Rules, the Biosimilar Guidelines and other applicable laws. The approval of carton and package insert is still pending. The defendant No. 3 is also likely to use data relating to the sales and therapeutic benefits of the plaintiffs' Trastuzumab (sold under the brand name HERCEPTIN., HERCLON. and BICELITIS.) in order to publicise the defendant's drug and create a market for such drug.

8.6 The wrongful use and/or reproduction of data relating to the plaintiffs' Trastuzumab by defendant No. 3 cannot be permitted since it will (i) deceive patients and/or doctors that data relating to clinical trials and safety and efficacy of the plaintiffs Trastuzumab is applicable to defendant's drug; (ii) amount to infringement of the plaintiffs' copyright in the package inserts for HERCEPTIN., HERCLON. and BICELITIS.; and (iii) result in inappropriate and potentially unsafe switching of patients from one product to another.

8.7 The defendant No. 3 has absolutely failed to establish similarity between its drug TrastuRel and the plaintiffs' Trastuzumab as required under applicable law in India. TrastuRel therefore cannot be considered biosimilar to the plaintiffs' Trastuzumab and should not have been approved as such by defendant No. 1.

Defendant No. 3's claims to the contrary are false and misleading.

8.8. It is mandatory for manufacturers of biosimilar drugs to establish similarity with the innovator biological drug at each stage of product development and testing, namely in product characterisation, preclinical (i.e., animal) trials and clinical (I.e., human) trials. It is only after a biological drug establishes similarity with the innovator biological drug on each of these steps/ parameters, can it be referred to as a 'biosimilar' drug. Strict adherence to step-wise generation and verification of data in accordance with applicable law in India is required before an approval is granted to a biosimilar drug.

8.9 Even under international standards, purported biosimilar drugs are assessed in a step-wise manner tor clinical efficacy, immunogenicity and safety through valid and comprehensive preclinical and clinical studies before marketing approval for such drugs as biosimilars is granted.

Written-Statement by Defendant No. 1

9. Written statement on behalf of the defendant No. 1 was filed wherein it is stated that all the necessary tests so as to establish the efficacy, safety and comparability have been conducted by the defendant No. 3 and same has been approved by the Committee of experts in the field of oncology after going through all the relevant data submitted by the defendant No. 3. The said Committee has reached a conclusion that the defendant No. 3's drug is efficacious, safe and similar to the plaintiffs drug. This Court in such a scenario, that too in a suit, will not go into the merits and decision of experts only for the reason that the plaintiffs claim that the drug is not a biosimilar drug.

9.1 The procedure in the present case started in the year 2009 after the initial license was issued for the purpose of examination, test and analysis. Thereafter, based on the data generated and by examining the comparability study of the defendant No. 3's drug with that of plaintiffs' drug, RCGM granted permission to defendant No. 3 to conduct pre clinical toxicological studies on 18th November,2010. On 28th July, 2011, RCGM based on pre clinical toxicological studies directed defendant No. 3 to approach defendant No. 1 for conduct of

clinical trials. Defendant No. 1 thereafter on 29th October, 2012 after being satisfied with the data so submitted granted permission to defendant No. 3 to conduct Phase-III clinical trials. And finally based on the data so generated from the trials the permission to manufacture was granted on 2nd June, 2015. The grant of manufacture was followed by the discussions and considerations of data by the expert committees such as NDAC (New Drug Approval Committee)/SEC(Subject Expert Committee),Technical Committee and Apex Committee.

9.2 The data generated over the years was examined by the experts at various stages and only after those experts were satisfied about the efficacy, safety and comparability of the defendant No. 3's drug that a permission to manufacture was granted.

9.3. It is submitted that the plaintiff is a third party in the entire process of grant of permission by the defendant No. 1 to defendant No. 3 and does not have any cause of action or locus so as to maintain the present suit for injunction. It is an admitted case that a drug in question is entitled to be called a similar biologic drug and plaintiffs drug is only a reference drug and hence no right of the plaintiff, in the entire process, has been infringed. Even assuming without that the proper procedure has not been followed, the same cannot be challenged by the plaintiff, being not an aggrieved party to the process. The suit is otherwise not maintainable due to availability of the alternate remedy under Rule 122 DC which provides for filing of appeal against any order passed by the answering defendant under Part XA of the Act.

9.4. It is stated that the grant of approval to manufacture or import a new drug for clinical trial or marketing is governed by Part XA of the Drugs and Cosmetics Rules, 1945. The Act or the Rules nowhere specifically mention about either the generic or a biosimilar drug, however Form 44 in entry (2)(b) prescribes the situation specifically for approval or permission for manufacture of already approved new drugs.

Accordingly a permission to manufacture already approved drug can be granted by the defendant No. 1. The manufacturer seeking to manufacture a similar drug

can rely upon the data of the innovator as available in the public domain and after establishing the safety and efficacy as required in Schedule Y either by relying upon the data or by generating relevant data can seek the permission to manufacture such a new drug which is already approved earlier. The specific requirement for conducting Phase III trial in Indian population comes from Schedule Y.

9.5 There is no specific requirement in the rules for conduct of Phase I or Phase II trial for the approval of the drug already approved outside the country when an applicant applies for approval of such drug in India as it is apparent from Appendix IA, Schedule Y that the data required for grant of permission to manufacture a new drug, which is already approved in the country, is significantly less than the data which is required for permission to manufacture a new drug for the first time in the country. Appendix IA, in fact, does not mention the necessity for conducting any trial, if the drug to be manufactured is already approved in the country.

9.6 The need for conducting Phase-III trial for the new drug approved outside India is primarily to generate the evidence of efficacy and safety of the drug in the Indian patients. Even the need for Phase III trials can be waived as has been done many cases as per the provisions of Rule 122(B)(3) and Schedule Y (1)(3). Appendix IA titled as data required to be submitted by an applicant for the grant of permission to import and/or manufacture a new drug already approved in the country is a specific appendix laid down for such a category of drugs. It also talks about data to be submitted where the conduct of any phase of clinical trial is not specified.

9.7 It is also alleged that under the provisions of Schedule Y (1)(3), for the drugs indicated in life threatening / serious diseases or the diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirement may be abbreviated, deferred or omitted as deemed appropriate by the Licencing Authority as mentioned under Rule 21(b).

9.8. The current Procedures followed for Grant of approval to manufacture and / or import new drugs including vaccines and Recombinant DNA derived products are governed under the regulatory provisions as provided in the Drugs and Cosmetics Act, 1940 and Drugs and Cosmetics Rules, 1945. Specifically, the definition of

"new drug" has been specified in Rule 122E of Drugs and Cosmetics Rules while the requirements and guidelines for permission to Import and / or Manufacture of new drugs for sale or to undertake clinical trials are specified in Rule 122A, 122B, 122D and Schedule-Y of the Rules.

9.9. Schedule-Y prescribes detailed requirements and guidelines for permission to import and/or manufacture of new drugs for sale or to undertake clinical trials. There is a specific provision in the Schedule under which the toxicological and clinical data requirements for grant of permission of new drugs or to undertake clinical trials, may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.

The defendant No. 3's application for manufacture of its drug was in conformance with the statutory requirements as contained in the relevant rules read with schedule Y along with the data on their drug trastuzumab and its physico chemical characterisation being comparable to the innovator product including its structure and other properties.

9.10. The proposal of the defendant No. 3 for grant of permission to manufacture and market Trastuzumab injection was referred to members of the SEC. The committee deliberated the matter in detail in its meeting held on 07.05.2015 and the report of this study which was conducted in 20 sites across India. Overall 106 patients were randomised in to the study, 84 subjects in the TrastuRel arm and 22 subjects in Herceptin arm. That the SEC in its meeting held on 7th May, 2015 evaluated the details of the data and recommended to the defendant for grant of manufacturing permission.

Based on the data submitted and the SEC recommendations, the application was further reviewed by the defendant and as per the provisions of Drugs and Cosmetics Rules, the application of M/s. Reliance was considered and permission to manufacture and market the drug Trastuzumab injection 150 mg/vial and 440 mg/vial Trastuzumab Bulk was granted on 2nd June, 2015.

10. It is admitted by the defendant No. 1 that under the Drugs and Cosmetics Act and Rules made there under, the term "Similar Biologies" has not been defined.

However, the Defendant No. 1 along with the Department of Bio - Technology has prepared "Guidelines on Similar Biologies: Regulatory Requirement for Marketing Authorisation in India" in the year 2012. The guidelines are not statutory under the Drugs and Cosmetics Act and the Rules made there under.

11. Reply has been filed on behalf of the defendant No. 3 to the plaintiffs' application under Section 94 red with Order 39, Rule 1 and 2 CPC. In the pleadings of defendant No. 3, it appears that many pleas are same as taken by the defendant No. 1 in its written statement. Thus, the same have not been repeated for the sake of brevity.

Reply by Defendant No. 3 i.e. Main Defendant

12. It is submitted on behalf of defendant No. 3 that the plaintiffs have no enforceable right in the drug Trastuzumab. The plaintiffs' patent with respect to the drug Trastuzumab lapsed in the year 2013. The defendant No. 3 is entitled in law, to rely upon the plaintiffs' data with respect to Phase I and Phase II trials, as available in public domain. The plaintiffs cannot seek either to restrain the defendant No. 3 from relying upon such data or against the defendant No. 1 from granting approvals on the basis of such publicly available data.

12.1 The plaintiffs are unable to specify any rights that are bring infringed by the defendant No. 3 by manufacturing and marketing a biosimilar of Trastuzumab. In fact the plaintiffs are challenging the approvals granted by the defendant No. 1 to the defendant No. 3 in order to retain their patent monopoly beyond the period granted to them under law in order to ensure sale of the drug on high prices.

12.2 The plaintiffs cannot, in the Ordinary Original Civil Jurisdiction of this Court, question and challenge the permissions granted by the defendant No. 1 to the defendant No. 3. The civil court is not an appropriate forum to consider, review or adjudicate over the decision of the defendant No. 1 to grant approvals to the defendant No. 3. Any challenge to an order passed by the defendant No. 1 can be appealed against to the Central Government under Rule 122DC of the Rules, 1945. The plaintiffs have not directly challenged the order of the defendant No. 1, have now challenged the same by way of filing the present suit. The present suit is

not maintainable as the jurisdiction of a civil court can be expressly or impliedly barred.

12.3. The plaintiffs do not have any civil right in the drug Trastuzumab and cannot prevent the defendant No. 3 from using the plaintiffs' data for manufacturing and marketing purposes, therefore once a patent has lapsed, the invention, i.e., the subject matter of the said patent, falls into public domain and the same can be appropriated by another party. The plaintiffs' patent for Trastuzumab lapsed in the year 2013. Indian jurisprudence does not recognise the concept of data exclusivity, therefore, the plaintiffs cannot claim any right with respect to Trastuzumab and its data thereof. The plaintiffs do not have any right in the name Trastuzumab' and cannot prevent the defendant from using the term thereof.

As the defendant No. 1 and other appropriate authorities have granted approvals to the defendant No. 3 as a biosimilar Trastuzumab, therefore defendant No. 3 is entitled to manufacture and market its drug under the same. It is submitted that to allow the plaintiffs to claim a right over the name Trastuzumab' and thus seek an injunction retraining the defendant No. 3 from manufacturing and marketing under the said name would be that this Court is sitting in judicial review of the approvals granted by the defendant No. 1.

12.4. The defendant No. 3 has, since the year 2009, conducted all the requisite studies, tests and trials and has obtained all the necessary approvals as per law for launch of its drug TRASTUREL which is a biosimilars version of Trastuzumab. It is submitted that the defendant No. 3 has produced all required pre-clinical tests, clinical trials as also the product literature, package insert, labels and cartons for approval. The approvals have been granted to the defendants after following due procedure as prescribed under the Act, Rules and Guidelines. The quality, efficacy and safety of the defendant's drug, TRASTUREL, has been evaluated by the Technical and Expert Bodies. The approval procedure adopted by the defendant No. 1 involved the regular review and evaluation of data submitted by the defendant No. 3 by various authorities such as the Institutional Bio Safety Committee (IBSC), the Review Committee on Genetic Manipulation (RCGM), the Drugs Controller General of India (DCGI), the Subject Expert Committee (SEC) as

well as by various Ethics Committees established by various hospitals in India and the State Licensing Authority.

12.5. The Biosimilar Guidelines, 2012 provide a regulatory pathway for approval and the approvals obtained by the defendant No. 3 are in accordance with the Act and the Rules. Under Rule 122E, an r-DNA drug is categorised as a new drug. Therefore, the stepwise regime for seeking approval for a new drug flows through the Guidelines, the Drugs and Cosmetics Act, 1940 and Rules thereof.

12.6. It is alleged that under the Drugs and Cosmetics Act, 1940 and the Rules thereof, there is a clear discretion vested with the defendant No. 1 to allow the abbreviation or omission of Phase I and Phase II clinical trials under Schedule Y and to rely upon the publicly available clinical trials data. It is only Phase III trials that are compulsory for such drugs under Schedule Y. It is submitted that the plaintiffs are attempting to mislead this Court by citing 1(iv)(a) of Schedule Y instead of 1(iv)(b). It is submitted that a clear distinction is provided between the two provisions as 1(iv)(a) is applicable for new drug substances discovered in India whereas 1(iv)(b) is for new drug substances discovered in countries other than India. The defendant No. 3's drug is a biosimilar of the reference drug and the reference drug was discovered by the plaintiff in a country other than in India.

13. Lastly, it is submitted that throughout the world it is a continued endeavour by relevant authorities as well as by the drug companies to discourage repeated human trials, when not necessary, as far as possible. This approach is substantiated by the fact that the plaintiffs themselves relied on their global clinical trials for seeking their approval for the drug Trastuzumab in India. Had it been the case that for each and every drug, in spite of having publicly available test data, a party, either being the innovator themselves or being any other party have to repeat all the clinical trials for each and every approval, in everycountry, then even the plaintiffs ought to have conducted Phase I, Phase II and Phase III clinical trials for their drug Trastuzumab when introduced in India.

14. The suit as well as the interim applications were listed before Court on 2nd November, 2015. As the drug in question was not launched by the defendant No. 3 and at that time even approval of package insert was granted, after small

hearing, the limited order was passed restraining the defendant No. 3 not to launch the drug in question.

15. The said order was challenged by the defendant No. 3 in appeal before the Division Bench in appeal, being FAO (OS) 625/2015 on 18th January, 2016, who disposed of the appeal in view of the reason that in the meanwhile the hearing in the interim application was concluded and order was reserved while mentioning that the I.A. No.23041/2015 be decided expeditiously as possible. The order passed by the Hon'ble Division Bench has not been informed by any party rightly so as the order was already reserved. The same was communicated by Administrative Officer from the office of the Registrar General after 8th February, 2016.

16. It is a matter of fact that most of the issues involved in the present case are similar with the facts in the suit, being CS(OS) No. 355/2014, wherein the injunctions applications and other applications were heard at earlier point of time. Thus, I consider appropriate to decide the pending applications in both the matters together.

17. Both parties have made their respective submissions on the basis of pleadings and documents produced. They have also filed the written submissions. The submissions of both parties on legal issues, reliance of decisions same as in earlier suit, being CS(OS) No. 355/2014.

18. After analysing the pleadings of the parties along with the documents filed therewith and submissions advanced by the learned counsel for the parties. For the sake of convenience, the following questions can be said to be sufficiently answering the contentions raised by the parties in the facts of the present matter:

i) Whether the plaintiffs have any right of action in the present case or not? If yes whether the suit is expressly or impliedly barred in law in view of the provisions of Drugs and Cosmetics Act 1945?

ii) If the suit is maintainable, whether this Court is within its powers to embark upon the approvals granted by the Drug controller in relation to the drugs in case it

impinges the civil rights of the plaintiff in order to protect the said civil rights or not?

iii) What is the impact of the Guidelines on Similar Biologics framed in the 2012 under the aegis of Drug Controller of India/ defendant No. 1 and the Government of India, Ministry of Bio technology and whether these guidelines would have any bearing in relation to the grant of the marketing and manufacturing approvals by the defendant No. 1 especially granted after the framing of the said guidelines or not?

iv) Whether the approval granted by the defendant No. 1 to defendant No. 3 by omitting the requirements of the clinical trials phase I and II would have any bearing upon the already granted approvals in the case of the similar biologics product or not and whether the defendant No. 3 has conducted all the clinical trials of drug as required under the strict provisions of the Act and Rules and Biosimilar Guidelines of 2012?

v) Whether the common law remedy can be pursued by the plaintiffs for misrepresentation and false information allegedly made by the defendant No. 3 in view of peculiar circumstances of the present case?

19. Maintainability/Jurisdiction of Civil Court:

Common Submissions on behalf of Defendants

a) The first objection raised by the defendants is with regard to the jurisdiction of Civil Court on the grounds that the Drugs and Cosmetics Act is a complete code itself. It is argued that there exists a bar to the jurisdiction of Civil Courts (having original jurisdiction) as the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the 'Rules') specifically provide for a mechanism of filing an 'Appeal' for challenging the Approvals granted under the Act. It is stated that Rule 122 DC as amended (the Drug Rules) and Section 37 of the Act as emended provide for a remedy to any person aggrieved by an order of the Licensing Authority. As the Act expressly provides for a mechanism for challenging the orders of the Licensing Authority, plaintiffs cannot be allowed to continue with the present proceedings before Civil Court. If the plaintiffs wanted to challenge the approval, they should

have filed a writ petition, the other remedy which is available to them. The suit is impliedly barred.

b) It is argued that if a civil court would start to examine the grant of Approvals, it will undermine and / or usurp the powers of the defendant No. 1 and its various constituents comprising of expert bodies and committees (Institutional Bio-safety Committee - IBSC, Review Committee on Genetic Manipulation - RCGM, New Drug Advisory Committee - NDAC and Technical and Apex Committees) who have examined and approved the drug before grant of manufacturing and marketing license under the Drugs Act and Rules.

c) Mr. Sanjay Jain, learned ASG, appearing on behalf of the defendants No. 1 and 2 and counsel for the defendant No. 3 referred the same following decisions:

a) State of A.P. v. Manjeti Laxmi Kantha Rao (dead) by Lrs and Others, (2000) 3 SCC 689.

b) Raja Ram Kumar Bhargava (dead) by Lrs. v. UOI, (1998) 1 SCC 681.

In these judgments, it has been laid down that the test adopted in examining such a question is (i) whether the legislative intent to exclude arises explicitly or by necessary implication, and (ii) whether the statute in question provides for adequate and satisfactory alternative remedy to a party aggrieved by an order made under it and wherever a right, not pre-existing in common law, in created by a statute and that statute itself provided a machinery for the enforcement of the right, both the right and the remedy having been created uno flatu and a finality is intended to the result of the statutory proceedings, impliedly barred."

d) He has also referred the decision of the Supreme Court in the case of Premier Automobiles Ltd. v. Kamlekar Shantaram Wadke and Ors., reported in 1976 1 SCC 496, wherein the plaintiffs, who were individual workmen suing in a representative capacity, filed a civil suit seeking a declaration that a certain Settlement Agreement arrived at between Premier Automobiles Ltd. and the Association Union under Section 18(1) of the Industrial Disputes Act, 1947 was not binding upon them and further for a permanent injunction restraining Premier

Automobiles from enforcing or implementing the terms of the impugned Settlement Agreement. The Supreme Court in this case observed as under, before giving its finding to the same effect at paragraph 23(3) of the judgment has held that the civil court will have no jurisdiction to try and adjudicate upon an industrial dispute if it concerned enforcement of certain right or liability created only under the Act. The civil court will have no jurisdiction even to grant a decree of injunction to prevent the threatened injury on account of the alleged breach of contract if the contract is one which is recognised by and enforceable under the Act alone be referring the quotation referred in Doe v. Bridges at page 859 are the famous and of-quoted words of Lord Tenterden, C.J. saying "Where an Act creates an obligation and enforces performance in a specified manner, we take it to be a general rule that performance cannot be enforced in any other manner."

e) Lastly learned ASG submits that the challenge to the grant of approval is available under Rule 122DC of the Drugs Rules. In the present case DCGI is the appropriate statutory authority to grant manufacturing and marketing approvals to new drugs under the Drugs Act. The plaintiffs have not availed of the remedy provided under Rule 122DC of the Drugs Rules to challenge the approvals granted to defendant No. 3. The nature of the reliefs sought by the plaintiffs cannot be granted by the Civil Court though a writ petition under Article 226 might be maintainable against a remedy available under a statute but a civil suit is barred.

f) In addition, it is argued by Ms. Pratibha M. Singh, learned Senior counsel for defendant No. 3, that the relief of injunction as claimed in the instant suit falls within the domain of the Specific Relief Act, 1963 and are discretionary reliefs which are circumscribed by the provisions of the Specific Relief Act and are to be available only when there is no alternative efficacious remedy available as the defendant No. 3 has been granted all the requisite approvals, as are required under law, for manufacturing and marketing its biosimilar drug TrastuRel, by the defendant No. 1. The said approvals have been granted after following due procedure as prescribed under the Act by the defendant No. 1 and the defendant No. 3's drug TrastuRel being evaluated under the stringent tests and procedures laid down under applicable laws.

g) The following decisions are referred by the senior counsel appearing on behalf of the defendants on this aspect:

i. N.D. Jayal and Anr. v. Union of India and Ors., (2004) 9 SCC 362

Para 20. "This Court cannot sit in judgment over the cutting edge of scientific analysis relating to the safety of any project. Experts in science may themselves differ in their opinions while taking decisions on matters related to safety and allied aspects. The opposing viewpoints of the experts will also have to be given due consideration after full application of mind. When the Government or the authorities concerned after due consideration of all viewpoints and full application of mind took a decision, then it is not appropriate for the court to interfere. Such matters must be left to the mature wisdom of the Government or the implementing agency. It is their forte. In such cases, if the situation demands, the courts should take only a detached decision based on the pattern of the well-settled principles of administrative law. If any such decision is based on irrelevant consideration or non-consideration of material or is thoroughly arbitrary, then the court will get in the way. Here the only point to consider is whether the decision-making agency took a well-informed decision or not. If the answer is "yes", then there is no need to interfere. The consideration in such cases is in the process of decision and not in its merits."

ii. Systopic Laboratories (Pvt.) Ltd. v. Dr Prem Gupta, 1994 Supp(1) SCC 160

Para 21: "As to whether clinical trials should have been conducted or not was primarily for the experts to decide and if the experts felt that in respect of the drugs in question such clinical trials were not necessary, it is not possible to hold that there has been no proper evaluation of the material that was submitted by the manufacturers before the Experts Committee"

h) It is submitted that the defendant No. 3 has not skipped Phase I trial as the objective of a Phase I trial is to establish comparative pharmacokinetics (pK) and this pK data was generated by defendant No. 3 as the initial part of the Phase III trial. Defendant No 2 did the Phase I and Phase II trials as part of the same sequential study since it was necessary to do the PK study in patients and not in

healthy volunteers. The Phase II study as dose finding and POC studies are not required for follow-on products (biosimilars or generics). The said justification was accepted by the defendant No. 1. The allegations of the plaintiffs that the approval was granted to the defendant No. 3 without conducting Phase I and Phase II trials is contrary to law.

Arguments addressed on behalf of Plaintiffs

20. On behalf of plaintiffs, similar submissions, as addressed in the suit, being CS(OS) No. 355/2014, are made. Mr. Rajiv Nayar and Mr. Sandeep Sethi, learned senior counsel appearing on behalf of the plaintiffs, inter alia, argued that since the approvals are contrary to the provisions of the Act, Rules and Guidelines of 2012 by Government, the defendants cannot be allowed to make misrepresentations to the doctors, hospitals and patients in the absence of requisite tests, the plaintiffs have no other remedy but to file the suit. They submit that despite of expiry of patent rights in 2013, the plaintiffs are manufacturing and marketing the drug in question and they are still market leaders in the entire world and the drug is one of the best drugs for the purpose of cancer treatment although they are not claiming data exclusively for comparison purposes at the time of obtaining the approval or any right on the molecule which was the subject matter of patent after its expiry. But the defendant No. 3 on the basis of said approvals is likely to destroy the business of the plaintiffs and would cheat the public at large by making misrepresentation in order to earn easy amount on the basis of spreading false information to the hospitals, doctors and patients providing the similar data and tests admittedly not conducted by them. Mr. Sandeep Sethi, learned Senior counsel, submits that the defendant No. 3 is time and again stressing that they are entitled to give all references of the plaintiffs by using of similar data. It is argued that the drug of the defendant No. 3 is not biosimilar. If the defendant No. 3 will manufacture and market the cancer drug without claiming bio-similarity, the defendant No. 3 is free to do so for which the plaintiffs have no objection.

It is also argued that once the defendant No. 3 is in violations of the rights of the plaintiffs and false information of biosimilar product in the public, the civil court has the jurisdiction to entertain the suit as the legal rights of the plaintiffs can only be

decided by the civil court who has the jurisdiction to pass the interim orders for illegal activities of the defendant No. 3 and the plaintiffs have become aggrieved party as the defendant No. 3 is insisting their product as reference product of the plaintiffs.

21. It is not disputed fact and agreed by both parties that in order to claim biosimilarity, a drug is required to be rigorously tested in strict accordance with the Drugs Act, the Drugs Rules and the Biosimilar Guidelines to establish that it is similar or near to similar to the innovator reference biologic on each of the parameters. The plaintiffs, who have challenged the process of approval as well as the validity of clinical trials, have given the details in the plaint in order to satisfy that all the requisite and mandatory tests have not been conducted. It is contended by the plaintiffs that the defendant No. 3 has failed to establish the biosimilarity of its drug TrastuRel for metastatic breast cancer with the plaintiffs' Trastuzumab on the following reasons:

a) Product characterisation studies: Defendant No. 3 did not conduct comparative product characterisation studies with the plaintiffs' Trastuzumab as required under Clauses 6,3.2, 6.3.3, 6.3.4 and 6.4 of the Biosimilar Guidelines. Only stand-alone tests seem to have been conducted, which are not sufficient to establish similarity between the plaintiffs Trastuzumab and TrastuRel. In the absence of 'head to head' comparison at the product characterisation stage, TrastuRel cannot be approved by defendant No. 1 as a biosimilar version of the plaintiffs' Trastuzumab.

b) Pre-clinical studies: Defendant No. 3 did not conduct animal pharmacology tests in relation to TrastuRel as part of its preclinical studies, in violation of the provisions of paragraph 1(1) (ii) of Schedule Y, item 3 of Appendix 1 read with Appendix III and IV of Schedule of the Drugs Rules and Clause 7.2 of the Biosimilar Guidelines, as reflected in defendant No. 3's letters dated January 4, 2010, July 12, 2010 and May 4, 2011 and defendant No. 1's letter dated November 18, 2011.

Defendant No. 3 has also not conducted a study of immune responses (Immunogenicity) in animals in relation to TrastuRel prior to using TrastuRel in human clinical trials. Immunogenicity studies are essential and mandatory under

paragraph 1.6 of the Guidelines for Generating Pre-clinical and Clinical data for RDNA Vaccines, Diagnostics and Other Biologicals, 1999, read with item 2.5 of Appendix I of Schedule Y of the Drugs Rules and Clause 7.3 of the Biosimilar Guidelines.

c) The letter to defendant No. 1 dated July 12, 2010 reflects that defendant No. 3 has also not conducted comparative pre-clinical studies with the plaintiffs' Trastuzumab as required under Clause 7 of the Biosimilar Guidelines. In the absence of comparative pre-clinical studies, TrastuRel cannot be approved by defendant No. 1 as a biosimilar version of the plaintiffs' Trastuzumab.

d) Phases I and II of clinical trials: Rule 122DA of the Drugs Rules mandates that all three phases of human clinical trials be conducted for a 'new drug' (as defined under Rule 122E of the Drugs Rules). Paragraph 2(7)(i) of Schedule Y of the Drugs Rules further provides that clinical trials should be conducted in a sequential manner, i.e., the data generated in Phase I clinical trials should form the basis of Phase II clinical trials and similarly, the data generated in Phase I and Phase II of the clinical trials should form the basis of Phase III clinical trials. Also, under paragraph l(l)(iv) of Schedule Y of the Drugs Rules, for new drug substances discovered in India, clinical trials are required to be carried out in India from Phase 1 onwards. Further, Clause 8 of the Biosimilar Guidelines mandates that all three phases of human clinical trials must be carried out for a biosimilar drug. Therefore a biosimilar drug is required to be subject to the full rigour of all phases of clinical trials, as envisaged under the Drugs Act read with the Drugs Rules and the Biosimilar Guidelines.

On October 29, 2012, defendant No. 1 approved a clinical trial protocol submitted by defendant No. 3 in relation to TrastuRel (the "defendant's CTR"). Such protocol was registered with the Clinical Trial Registry of India (the "CTRI") by defendant No. 3 on April 12, 2013 (registration No. CTRI/2013/04/003549). The defendant's CTR reflects that TrastuRel was allegedly tested for efficacy and pharmacokinetics end-points on 105 patients with solely HER 2+ metastatic breast cancer. Further, the defendant's CTR purportedly relates solely to Phase III clinical trials and admittedly no Phase I and Phase 11 clinical trials have been conducted by

defendant No. 3 for TrastuRel.

e) Under applicable law. Phase III studies are intended to confirm the evidence accumulated in Phase II clinical trials effectiveness of the drug. Skipping phases of clinical trials is not scientifically justified under Rule 122DA and Paragraph 2(7)(i) of Schedule Y of the Drugs Rules, which mandate sequential clinical trials. Further Paragraph l(iv)(a) of Schedule Y of the Rules clearly states that 'for new drug substances discovered in India [TrastuRel], clinical trials are required to be carried out in India right from Phase I and data should be submitted as required under Items 1, 2, 3. 4, 5 (data, if any, from other countries) and 9 of Appendix I.

f) In its application for manufacturing approval in Form 44 of the Drugs Rules to defendant No. 1 (the Form 44 Application), defendant No. 3 states that its application does not relate to subsequent approval for an already approved new drug. Accordingly, contrary to the submissions of defendant No. 3, no abbreviation of clinical trials was applicable to TrastuRel.

g) In its meeting dated September 19, 2012, the New Drugs Advisory Committee (the "NDAC") had recommended defendant No. 3 to submit pharmacokinetic data relating to TrastuRel to the defendant No. 1 prior to conducting the "second part of the study", clearly indicating that the different phases of clinical trials were to be conducted separately. Such recommendation was further endorsed by the Technical Committee on March 27, 2014 as well as the Apex Committee on April 15, 2014.

h) Despite the above referred directions of the NDAC, Technical Committee and Apex Committee, defendant No. 3 sought to conduct only Phase III clinical trials pursuant to its application to defendant No. 1 dated 16th February, 2012. Under paragraph 2(6) of Schedule Y of the Drugs Rules and item 5 of Appendix I and Clause 8.1 of the Biosimilar Guidelines, a Phase I clinical trial, which may be conducted in healthy volunteer subjects or certain types of patients, should include end points to test pharmacokinetics, pharmacodynamics, maximum tolerated dose and early measurement of drug activity. An important objective in Phase 11 clinical trials is to explore the dosage of the proposed drug. Since a biosimilar is never identical to the reference biological product, in the absence of separate and

independent Phase I and Phase II clinical trial for TrastuRel, it is grossly inaccurate to assume that the Phase I and Phase II data for TrastuRel would be the same as the plaintiffs' Trastuzumab,

i) According to the letter dated July 28, 2011, the Review Committee for Genetic Manipulation (the "RCGM") directed defendant No. 3 to approach defendant No. 1 to obtain approval for conducting clinical trials for TrastuRel, and contrary to defendant No. 3's submissions, did not recommend the skipping of any phases of clinical trials. Accordingly, directly carrying out Phase III clinical trials by defendant No. 3 is completely unwarranted. Further, no RCGM approval was sought to waive Phases I and II of the clinical trials except the defendant No. 3 had informed that it was not required.

Phase III of clinical trials: The defendant's CTR states that its primary outcome is efficacy assessed as the end point of Objective Response Rate (ORR). The end points in the defendant's CTR are contrary to the specifications under the Drugs Act read with the Drugs Rules and Biosimilar Guidelines. Under paragraph 2(8)(i) of Schedule Y of the Drugs Rules, Phase 111 clinical trials confirm the therapeutic benefits and the safety and efficacy of the drug. Further, under Clause 8.3 of the Biosimilar Guidelines, confirmatory safety, efficacy and immunogenicity clinical trials to demonstrate the similarity in safety and efficacy profiles of the purported biosimilar and the innovator biological drug are critical for the approval of a biological drug as a 'biosimilar'.

j) According to the defendant's CTR, safety studies were only a secondary objective in the clinical trials purportedly conducted by defendant No. 3, and immunogenicity studies were not conducted at all.

k) The defendant's CTR reflects that TrastuRel was proposed to be tested on a sample size of only 105 patients. Further, merely 84 were tested with TrastuRel and only 53 of such subjects completed the 25-week evaluation phase of the study (package insert for TrastuRel handed over by defendant No. 3 on November 2, 2015). The number of subjects tested with TrastuRel is grossly inadequate for a Phase III clinical trial. It is an established practise that the sample size for a Phase III clinical trial, which is required to test the safety, efficacy and immunogenicity of

a drug, is considerably larger than the sample size for a Phase I clinical trial, where the primary end point of the clinical trial is pharmacokinetics. Since the purpose of these tests is, inter alia, to determine the adverse effects of a biological drug in the actual patient population, a larger sample size is required to be able to determine as many possible side effects as may be mapped during the course of the trial. Apart from being insufficient to test the safety and immunogenicity of a biological drug, a sample size of 105 patients (with only 53 patients having completed the ORR trial) is not sufficient for ORR as the primary end point, which requires a statistically significant sample size. It is submitted that sample size for a particular phase of clinical trial is required to be determined by expert biostatisticians and no such experts appear to have been part of the NDAC which approved the defendants' CTR and subsequently the clinical trial results.

l) Despite legal requirements and directions, defendant No. 3 did not conduct Phase 1 and Phase II clinical trials for TrastuRel, and the Phase 111 clinical trial purportedly conducted was not in accordance with applicable law.

m) In its application in Form 44 of the Drugs Rules dated March 27, 2015 to defendant No. 1, defendant No. 3 sought manufacturing authorisation for TrastuRel for all the Indications despite having conducted clinical trials only on patients with HER2+ metastatic breast cancer. On the basis of such application, the Subject Expert Committee (Oncology and Hematology) (the "SEC") recommended the grant of marketing authorisation to TrastuRel on May 7, 2015 (the "SEC Recommendation") TrastuRel for all the Indications despite the defendant's CTR reflecting that tests were conducted only on patients with HER2+ metastatic breast cancer.

n) Defendant No. 3 was required to conduct detailed pre-clinical and clinical trials for the approval of TrastuRel for any new indication since under Rule 122E(b) of the Drugs Rules, a drug already approved by defendant No. 1 which is proposed to be marketed for anew indication, is a "new drug" for the purposes of the Drugs Rules.

Approval of such a "new drug" requires complete pre-clinical and clinical trials to be conducted by the applicant drug manufacturer. Defendant No. 3 has admittedly

not undertaken any clinical trials for the Additional Indications, in complete violation of the Drugs Rules and Biosimilar Guidelines.

o) In terms of Clause D of Form 44 of the Drugs Rules, which form is required to be filed, inter alia, along with applications for approval for manufacture of new drugs, the applicant should provide therapeutic justification for the new claim and the data generated on safety or quality parameters. The Form 44 Application states that such application does not relate to subsequent approval for new indications and, accordingly, admittedly, no such therapeutic justification or data has been provided by defendant No. 3.

p) Extrapolation of the clinical data relating to one therapeutic indication to another different indication is not automatic or unqualified and must be therapeutically justified with safety and quality data. Such extrapolation is not justified in the case of TrastuRel for the Additional Indications because the end-points for a clinical trial for metastatic stage cancer are different from the end-points for an early stage cancer, including in relation to the safety and efficacy. In particular, it is an accepted medical fact that metastatic breast cancer cannot be cured, it can only be treated to prolong the patient's life; therefore, the drugs targeting metastatic breast cancer aim to control the growth of the cancer and/or to relieve symptoms caused by it. Conversely, early breast cancer can be cured in some cases. Accordingly, the appropriate clinical trial end points for a drug targeting HER2+ early breast cancer is disease free survival, which measures the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer. Disease free survival cannot be the end point for HER2+ metastatic breast cancer.

q) There is no material on record to show that TrastuRel has never been tested to ascertain if it can cure cancer, since the defendant's CTR is restricted to patients suffering from the incurable HER2+ metastatic breast cancer. Accordingly, the results of clinical trials purportedly conducted on TrastuRel in relation to HER2+ metastatic breast cancer cannot be relied upon by defendant No. 3 for approval of the TrastuRel for the Additional Indications. International practices do not permit immunogenicity data in immunosuppressed subjects to be extrapolated to an

indication in healthy subjects or patients with autoimmune diseases, and therefore, data from HER 2+ metastatic breast cancer relating to tests conducted with immunosuppressed subjects cannot be extrapolated to HER2+ early breast cancer.

r) For clinical trials in relation to HER 2+ metastatic breast cancer, the patient population is heterogeneous, which adversely affects the clinical outcome. On the contrary, clinical trials for HER2+ early breast cancer would be conducted on a homogeneous patient population, which would be a sensitive clinical trial test model to show the potential differences with the innovator biological drug. It is this scientifically appropriate setting which allows the identification of data from a treatment-free follow-up phase which is crucial for the comprehensive characterisation of the immune response.

s) Defendant No. 3 has not used a sensitive clinical trial test model which could detect potential differences between TrastuRel and the plaintiffs Trastuzumab. HER 2+ metastatic breast cancer is not a sensitive clinical trial test model to detect potential differences in safety, efficacy and immunogenicity. The pharmacokinetics is severely affected because of the patent's health status and tumor burden. The SEC Recommendation for the Additional Indications in the above referenced circumstances discloses failure to follow the legal procedures in approving drugs in India, which is, inter alia, the basis of the present proceedings and displays an unfortunate apathy towards public health and safety. In this regard, it is also significant that the approval of the plaintiffs' Trastuzumab, which is the innovator drug in the present case, for the Additional Indications in India took almost four years and eight years respectively after the initial approval for HER2+ metastatic breast cancer and was based on global clinical trials conducted by the plaintiffs.

t) The findings of the SEC Recommendation are not based on the clinical trials purportedly conducted by defendant No. 3 in relation to TrastuRel since the defendant's CTR clearly stated that studies were purportedly only conducted on patients with HER2+ metastatic breast cancer, while the SEC has inexplicably recommended TrastuRel for the Additional Indications, as well. Accordingly, defendant No. 1 should be enjoined from acting in furtherance of the SEC

Recommendation and from granting marketing authorisation to TrastuRel. The SEC has made no observation in relation to the safety and efficacy of TrastuRel.

u) In order to be considered biosimilar to the plaintiffs' Trastuzumab, TrastuRel is required to be tested for all the Indications that the plaintiffs' Trastuzumab is capable of treating, i.e. HER 2+ metastatic breast cancer, HER 2+ metastatic gastric cancer and HER 2+ early breast cancer. As stated above, the defendant's CTR reflects that the TrastuRel is not tested for the Additional Indications, i.e. HER 2+ metastatic gastric cancer and HER 2+ early breast cancer. TrastuRel cannot be considered to be biosimilar to the plaintiffs' Trastuzumab in the absence of the requisite trials for all the Indications.

v) Defendant No. 3 sought approval from defendant No. 1 for the carton, label and package insert for TrastuRel pursuant to its letter dated October 20, 2015. Subsequently, the package insert for TrastuRel was recommended for approval with certain modifications and conditions by the SEC on October 27, 2015 (the "Package Insert Recommendation"). Defendant No. 3 has not obtained the final approval of defendant No. 1 for the package insert for TrastuRel which is required under Clause l(l)(vi) of Schedule Y of the Drugs Rules. In the absence of the final approval of defendant No. 1 for the package insert of TrastuRel, defendant No. 3 cannot launch this drug in the market.

w) In view of the above, (a) the approval of the defendant's CTR by defendant No. 1 on October 29, 2012- (b) the clinical trials purportedly conducted by defendant No. 3 pursuant to the defendant's CTR; (c) the SEC Recommendation relating to the grant of a marketing authorisation to TrastuRel for all the Indications; (d) the subsequent grant of the Manufacturing Authorisation by defendant No. 1; and (e) the launch of TrastuRel in the absence of the above referenced marketing authorisation and package insert approvals would be in violation of the Drugs Act, the Drugs Rules and the Biosimilar Guidelines.

x) TrastuRel as claimed by defendant No. 3, has been developed for the treatment of all the Indications and it will compete directly with the plaintiffs' Trastuzumab. The defendant's CTR reflects that defendant No. 3 has purportedly conducted clinical trials to compare TrastuRel with HERCEPTIN. Further, as stated above,

the basis of the SEC Recommendation for the Manufacturing Authorisation was the alleged comparability of TrastuRel with the plaintiffs' Trastuzumab. Accordingly, the Manufacturing Authorisation for TrastuRel from defendant No. 1 is with respect to a purported biosimilar version of the plaintiffs' Trastuzumab/ HERCEPTIN.

y) As stated in the foregoing paragraphs, TrastuRel has not been sufficiently and adequately tested to be termed as a biosimilar product, as incorrectly claimed by defendant No. 3, and there are reasonable apprehensions regarding the safety, efficacy, immunogenicity and quality of TrastuRel. By unfairly and incorrectly referring to TrastuRel as a biosimilar or comparable version of the plaintiffs' Trastuzumab/HERCEPTIN. and, in turn, linking TrastuRel with plaintiffs' Trastuzumab/ HERCEPTIN. and, in turn, linking TrastuRel with the plaintiffs' Trastuzumab/ HERCEPTIN., any deficiency discovered in TrastuRel is likely to be imputed to the plaintiffs' Trastuzumab/ HERCEPTIN. This will lead to a dilution of the plaintiffs' global reputation and goodwill built over many years in relation to the plaintiffs' Trastuzumab, HERCEPTIN., HERCLON. and BICELITIS and cause irreparable injury to the plaintiffs.

z) The SEC Recommendation, granted on the basis of alleged comparability of TrastuRel with the plaintiffs' Trastuzumab, reflects that defendant No. 3 has misrepresented TrastuRel as similar and/or comparable to the plaintiffs Trastuzumab/ HERCEPTIN. As stated above, the defendant's CTR is not in compliance with the Drugs Act, the Drugs Rules and the Biosimilar Guidehnes. Defendant No. 3 has failed to establish comparability or biosimilarity between TrastuRel and the plaintiffs' Trastuzumab on the basis of tests purportedly conducted pursuant to the defendant's CTR and TrastuRel is not biosimilar to the plaintiffs' Trastuzumab.

22. On the basis of above referred reasons, it is submitted on behalf of the plaintiffs that TrastuRel has not been adequately and/or appropriately tested, inter alia, under the provisions of the Biosimilar Guidelines and that the approvals granted to defendant No. 3 are invalid and cannot be acted upon.

23. The plaintiffs in the injunction application sought the relief of injunction restraining defendant No. 3 from launching, introducing, selling, marketing and/or distributing the defendant's drug in the Indian market as 'Trastuzumab' or otherwise for any of the Indications, pursuant to the marketing authorisation to be granted by Defendant No. 1 or representing its drug Trastuzumab or a biosimilar version or from claiming similarity or relying upon or otherwise referring to the plaintiffs' trademarks HERCEPTIN., HERCLON. or BICELTIS., or any data relating to the plaintiffs' Trastuzumab marketed as HERCEPTIN., HERCLON. or BICELTIS. including data relating to its manufacturing process, safety, efficacy and sales, in any press releases, public announcements, package insert, promotional, sales, marketing or other material for the defendant's drug, including in subsequent applications to various regulatory authorities in relation to the defendant's drug, and from claiming any similarity with HERCEPTIN., HERCLON. or BICELTIS.;"

24. In case the prayer made in the application is examined, it is evident that the plaintiffs were seeking an injunction for launching, introducing the drug by the defendant No. 3, an injunction from representing as bio-similar products until appropriate tests and studies are conducted including guidelines on similar biologics and injunction from press releases and relying upon or referring to the plaintiffs trade mark claiming similarity of two drugs.

25. The plaintiffs have claimed that the defendant No. 3 is infringing their legal rights and will make a misrepresentation is they are allowed to use the data and to claim bio-similar product. Their main concern is that without establishing the safety and efficacy as required under the Act, Rules and Guidelines 2012, they are not entitled to claim that it is a biosimilar drug of the innovator and would not be entitled to use the data of the plaintiffs and give references in its package insert, carton and publicity materials by making the false statement and misrepresentation. Otherwise, independently, they are entitled to market drug in question without any such references. If the clinical trials are not conducted, the Regulatory Authority is liable to take action under Rule 122 DB. But if the references of biosimilar are made by the defendant No. 3 for promoting and selling the drug in question, the plaintiffs are entitled to file the suit. The decisions are

referred by the counsel for the plaintiffs. Even written-submissions filed on this point are almost same.

26. It is settled law that Section 9 of the Code provides that civil court shall have jurisdiction to try all suits of a civil nature excepting the suits of which their cognisance is either expressly or impliedly barred. To put it differently, as per Section 9 of the Code, in all types of civil disputes, civil courts have inherent jurisdiction unless a part of that jurisdiction is carved out from such jurisdiction, expressly or by necessary implication by any statutory provision and conferred on other Tribunal or Authority. Thus, the law confers on every person an inherent right to bring a suit of civil nature of one's choice, at one's peril, howsoever frivolous the claim may be, unless it is barred by a statute. Even as per the decision referred by defendant No. 1 in the case of State of Andhra Pradesh (supra) it is held that the normal rule of law that the civil courts have jurisdiction to try all suit and such exclusion is not readily inferred and the presumption to be drawn.

27. It is trite and debated time and again that the rule of pleadings postulate that a plaint must contain material facts. When the plaint read as a whole does not disclose material facts giving rise to a cause of action which can be entertained by a civil court, it may be rejected in terms of Order 7, Rule 11 of the Code. Similarly, a plea of bar to jurisdiction of a civil court has to be considered having regard to the contentions raised in the plaint if averments disclosing cause of action and the reliefs sought.

a) In Smt. Ganga Bai v. Vijay Kumar and Ors., (1974) 2 SCC 393, this Court had observed as under:

"There is an inherent right in every person to bring suit of a civil nature and unless the suit is barred by statute one may, at ones peril, bring a suit of one's choice. It is no answer to a suit, howsoever frivolous the claim, that the law confers no such right to sue. A suit for its maintainability requires no authority of law and it is enough that no statute bars the suit."

b) In Dhannalal v. Kalawatibai and Ors., (2002) 6 SCC 16, relying on the afore-extracted observation in Ganga Bai's case (supra), this Court had held as follows:

"Plaintiff is dominus litis, that is, master of, or having dominion over, the case. He is the person who has carriage and control of an action. In case of conflict of jurisdiction the choice ought to lie with (1974) 2 SCC 393 (2002) 6 SCC 16 the plaintiff to choose the forum best suited to him unless there be a rule of law excluding access to a forum of plaintiff's choice or permitting recourse to a forum will be opposed to public policy or will be an abuse of the process of law."

28. Originally the suit was filed as Quia Timet Action. It is settled law that such an action is maintainable. If a party fears or apprehends, then the injunction may be passed by the court on some threatened act being done in future, would cause him substantial damage where monetary relief would not be an adequate or sufficient remedy. In a quia timet action, the court passes an injunction as a preventive measure so as to prevent the future occurrence of the wrong on the basis that the reasonable apprehension of the injury to be occurred in future rather than waiting for the perfection of the wrong. In the case of Kuldip Singh v. Subhash Chander Jain andOrs., AIR 2000 SC 1410 in para 7 it is held that "A quia timet action is a bill in equity. It is an action preventive in nature and a species of precautionary justice intended to prevent apprehended wrong or anticipated mischief and not to undo a wrong or mischief when it has already been done. In such an action the Court, if convinced, may interfere by appointment of receiver or by directing security to be furnished or by issuing an injunction or any other remedial process "

29. It is not disputed by all that there is no specific bar of civil court jurisdiction in the Act and Rules. It is also admitted position that the main dispute is between the private parties i.e. plaintiffs and defendant No. 3. It is not denied by the defendants that the suit is not filed against any Government employees who were involved in the process of approvals. It is admitted by the defendant No. 1 that as per Act and Rules there is no procedure for cross-notice or to hear the grievances of the plaintiffs that the authority has not considered the clinical trials properly or to send the copy of the approvals and backed up documents who claimed himself as an aggrieved party.

30. In view of the attendant circumstances discussed above, I have already observed as to how the plaintiffs have an enforceable right to seek an interdict the court and the court can exercise the jurisdiction not merely on the basis of private lis between the parties but by invoking the public interest doctrine which also guide the courts, still, I am discussing the provisions of Section 9 of the Code of civil procedure in order to discuss the plea raised by the defendant in relation to the ouster of the jurisdiction. Section 9 of the Code of Civil Procedure ("CPC") mandates that civil courts have the jurisdiction to determine all disputes of a civil nature, unless their jurisdiction is barred under a statute, either expressly or by necessary implication. It is settled law that if the appropriate authority has acted in violation of the fundamental principles of judicial procedure that may tend to make the proceedings illegal and void, then Civil Court's jurisdiction may not be taken away which has under those circumstances have the jurisdiction to examine the non-compliance with such provisions of the statute. There is inherent right in every person to bring a suit of a civil nature unless the suit is barred expressly and impliedly. (See Dhulabhai v. State of Madhya Pradesh and Anr., (1968) 3 SCR 662, Abdul Gafur and Anr. v. State of Uttarakhand and Ors., (2008) 10 SCC 97, Dwarka Prasad Agarwal v. Ramesh Chander Agarwal, (2003) 6 SCC 220, Harbanslal Sahnia and Anr. v. Indian Oil Corporation and Ors., (2003) 2 SCC 107, State of Madhya Pradesh and Anr. v. Bhailal Bhai (1964) 6 SCR 261, State of Kerala v. Ramaswami Iyer and Sons, (1966) 3 SCR 582, Secretary of State v. Mask and Company, (1940 40 LR 222).

31. It is also settled law that the exclusion of the jurisdiction of the civil courts is not to be readily inferred, but that such exclusion must either be explicitly expressed or clearly implied. Even if jurisdiction is so excluded, the civil courts still have jurisdiction to examine into cases where the provisions of the Act have not been complied with, or the statutory tribunal has not acted in conformity with the fundamental principles of judicial procedure. If consequence of the same is that, it affects the civil right of the party, then the civil suit is maintainable. In the case of Mohammad Din and Ors. v. Imam Din and others, AIR 1948 PC 33 it laid down the principle that where the tribunals do not act in conformity with the fundamental rules of judicial procedure or where the rules of the law are not followed, the civil court has jurisdiction and to this extent no ouster can be inferred)

32. The decision in the case of Mohammad Din (supra) has been followed by the courts in India from time to time including the High Courts of Punjab and Haryana in the case of and also by Allahabad High Court recently in 2010 in the case of Shivdhesar Singh v. Union of India, (2011) 2 AWC 1202.

33. Applying the dictum of Mohammad Din (supra) which still holds the field and followed by the courts, the present suit cannot be said to be barred in the present form. I find that the judgments cited by Mr. Sibal on the breach of the statutory duty are also distinguishable in the facts of the present case as it is not merely the case of the breach of any statutory duty but also the violation of the rules of the judicial procedure by not following the guidelines framed by the controller on his own and granting the approvals on the basis of different regime in an undue haste when the Supreme Court order also mandated the conducting of the clinical trial. All this have the bearing on the rights of the plaintiffs giving them right to enjoin the defendants till the time the defendants accomplish the onerous task of seeking approvals as per the bio similar regime framed in the form of the guidelines.

Regime of Bio-Similar

34. Let me now deal with the latest trend of regime of Bio-similar drug. Admitted position is that when the patent for the original molecule expires, other companies can launch follow-on versions of the same. If the molecule is chemically synthesised, the follow-on molecule is called a "generic" whereas when the molecule is a biological (like a monoclonal antibody), the follow-on molecule is called a biosimilar. 'Generics' and 'Biosimilars' are developed by comparing their properties to the original molecule, which is called a reference product. Any follow-on biological product that is approved based on evaluation of comparative data to the reference product is called a biosimilar.

35. In view of the development and growth of the market for biosimilars in India and the international standards for approval of such products, the Guidelines on Similar Biologies were issued in 2012. These guidelines lay down specific standards for development and evaluation of similar biologies; these are in addition to the general standards for evaluation of new drugs that exist under the Drugs Act and the Drugs Rules and seek to ensure comparability of safety,

efficacy and quality between the innovator biologic and the biosimilar, prior to the approval of such biosimilar.

36. The Guidelines on Similar Biologics provide a detailed and structured process for comparison of the similar biologic with the reference biologic to test the safety, efficacy and immunogenicity of the similar biologic as against the reference biologic at each stage including the product characterisation, the pre-clinical studies and clinical trials. Under these guidelines demonstration of similarity of biologics is a sequential step-wise approach. This process is aimed at ensuring that the similar biologic is comparable inequality to the reference biologic and can be safely used in the treatment of specified disease or disorder.

37. After the issuance of the Guidelines on Similar Biologics on 15th September, 2012, all applications for manufacturing and marketing authorisation of similar biologies in India are required to be evaluated on the basis of the standards set forth in the Guidelines on Similar Biologies. The Guidelines on Similar Biologies ensure that adequate tests are conducted prior to the approval of biosimilars. These may not be statutory in nature but as per guidelines of the Government from time to time, it is essential that they are also followed at all stages in order to ensure the safety of patients. In the case of life saving drugs, no one can deny that at thorough consideration should be given to the scientific basis of the study design, objectives, study end-points, sample sizes and study duration of the applicant's product before approval is granted under the Guidelines on Similar Biologics and only products which have been approved under the Guidelines on Similar Biologics should be allowed to be represented as biosimilar products. The said 2012 Guidelines provide that similar biologics are regulated as per the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945 so that the approval of biosimilar products of parties must satisfy all the stringent regulatory requirements before manufacturing and marketing its product.

38. The 2012 Guidelines provide that similar biologics are regulated as per the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945. In nutshell, the 2012 Guidelines stipulate that the approval of biosimilar products of a party must satisfy all the stringent regulatory requirements and having been duly

approved is entitled to manufacture and market its product.

39. The Biosimilars have existed even prior to the 2012 Guidelines and then the application of the applicant was to be tested on a case by-case evaluation governed under "Notification Regarding Adoption of The Recommendations of The Task Force On R-Pharma Under The Chairmanship of Dr R A Mashelkar, DG-CSIR With Effect From 1.4.2006".

40. I have seen the Mashelkar Committee Report relied upon by the defendants and the said report appears to give some indication as to development of LMO (which is living modified organism) by way recombinant DNA technology. The report provides certain protocols for the development of indigenous product where end product is LMO which is starting point for someone who is attempting to development Living modified organism. To that extent, the defendant No. 3 is right that the concept and mechanism to take approval of the biotechnology products and artificially engineered modified genetic sequences was available. But, by placing reliance on the said report to say that the biosimilar guidelines were already in place and the new guidelines have no role to play wherein an applicant/ defendant engineers his own biological compound and attempts to ascribe the same quality, efficacy, safety norms, dosage, potency of the compound with other characteristics same as the base compound which means that two persons are artificially engineering the genetic sequencing arriving at the same conclusion and also the same characteristics so as to call their products as clones or biologically similar to each other was not specifically provided for in the Malshekar report and if so provided still the guidelines operate in the field which regulate the entire process of the study of the biosimilar products prior to the grant of the approval and fill the gaps in the entire regulatory procedure of the grant of the approval of bio similar by insistence of the clinical trials and other relevant steps which were not earlier not provided for by looking from greater degree of care and attention as is evident from that of the preface of the guidelines.

41. Thus, even if the starting point of the discussion in guidelines on similar Biologics of 2012 is Malshekar report, still, the defendant's plea that the system was already placed on the date of approval of drug of the defendant No. 3 and the

bio similar were already approved on the face of it a contradictory argument by defendant No. 1 especially when the defendant No. 1 is the head of the CDSCO (Central Drugs Standard Control Organisation) which is the central drug authority under the Act and has passed the guidelines with the close connection with Ministry of Science and Technology. The defendant No. 1 by authoring the guidelines to say that the said biosimilars are to be treated distinctly with greater degree of care and circumstance as against the ordinary regime of bio-equivalence cannot justify the contrary position by urging that the guidelines have no role to play or are not statutory in character and thus can be conveniently bypassed as non binding or there is nothing new about the approvals in biosimilar products as they were being granted earlier. All these stands are contradictory to the preface of the guidelines to which the defendant No. 1 is participant and thus cannot plead to contrary before this court.

42. As regard binding nature of the guidelines, it is well settled principle of law that the guidelines are in the nature of the directions issued by the Government and till the time the said guidelines and directions are not in contradiction but are mere addition to the already existing rules and regulations, it cannot be said that the said guidelines are not having legal validity and are not required to be adhered to being non binding in character.

43. The reference is invited to the case of Bant Singh v. Man Singh, AIR 1976 PandH 102, wherein the Division Bench of the High Court observed thus:

"There are no rules which may regulate the supply of canal water for gardens and orchards. The rules which are in existence make a provision for regulating the supply of canal water to lands only, The Government in its wisdom thought of issuing some instructions for the purpose of regulating extra supply of canal water for gardens and orchards and those instructions with suitable amendments made off and on, bold the field till today. Obviously, these instructions were issued to supplement the rules in existence, which were silent on the question of supply of canal water to the gardens and orchards. By issuing these instructions, a complete and detailed procedure has been prescribed for the supply of canal water for the gardens and orchards. These instructions do in no way amend, supersede or alter

the existing rules; rather the same have the effect of filling the gap and supplementing the existing rule."

(Emphasis Supplied)

44. Likewise, it is also a settled law that the guidelines / directions issued by the department though not statutory but are in contravention to the provision of the Act and rules framed thereunder cannot be said to be not to be complied with or non enforceable by the court of law. The Supreme Court in the case of Virendra Hooda v. State of Haryana, AIR 1999 SC 1701 observed as under:

"The view taken by the High Court that the administrative instructions cannot be enforced by the appellant and that vacancies became available after the initiation of the process of recruitment would be looking at the matter from a narrow and wrong angle. When a policy has been declared by the State as to the manner of filling up the post and that policy is declared in terms of rules and instructions issued to the Public Service Commission from time to time and so long as. These instructions are not contrary to the rules, the respondents ought to follow the same."

(Emphasis Supplied)

45. The Constitution Bench of Supreme Court in the case of Sant Ram Sharma v. State of Rajasthan, (1968) IILLJ 830 SC, has pointed out at p. 1914 SC that the Government cannot amend or supersede statutory Rules by administrative instructions, but if the rules are silent on any particular point Government can fill up the gaps and supplement the rules and issue instructions not inconsistent with the rules already framed.

(Emphasis Supplied)

46. The aforesaid ruling of Sant Ram(supra) has been reiterated in paragraph 9 of the judgment by a three Judge Bench of Supreme Court in the case of Union of India v. K.P. Joseph, [1973] 2 SCR 752, as under:

Generally speaking, an administrative Order confers no justiciable right, but this rule, like all other general rules, is subject to exceptions. This Court has held in Sant Ram Sharma v. State of Rajasthan and Anr., (1968) IILLJ 830 SC, that although Government cannot supersede statutory rules by administrative instructions, yet, if the rules framed under Article 309 of the Constitution are silent on any particular point, the Government can fill up gaps and supplement the rules and issue instructions not inconsistent with the rules already framed and these instructions will govern the conditions of service.

(Emphasis Supplied)

47. From the reading of the aforementioned observations of Supreme Court in the case of the Sant Ram (Supra) and also K.P. Joseph (supra), it is clear that the administrative orders, directions or guidelines do not create any justiciable right is a rule not without exception and in the cases where the guidelines are framed with aim to fill the gaps in the legal framework or regulatory measures or are supplemental rules, the courts can proceed to enforce them in the form of legally justiciable right in such circumstances. The law laid down in the case of Sant Ram (supra) and K.P. Joseph (supra) has been further given imprimatur of Supreme Court in the case of Dhananjay Malik v. State of Uttaranchal, (2008) 4 SCC 171.

48. It is also trite law that the judicial interference is permissible in the cases the deviations from the guidelines so framed by the Government are fundamental in nature and is totally contrary to the object sought to be achieved by the said guidelines and directions issued and the public interest so required. In the case of Narendra Kumar Maheshwari v. UOI, AIR 1989 SC 2138, the Supreme Court observed thus:

"The Court would be inclined to perhaps overlook or ignore such deviations, if the object of the statute or public interest warrant, justify or necessitate such deviations in a particular case. This is because guidelines, by their very nature, do not fall into the category of legislation, direct, subordinate or ancillary. They have only an advisory role to play and nonadherence to or deviation from them is necessarily and implicitly permissible if the circumstances of any particular fact or law situation warrants the same. Judicial control takes over only where the

deviation either involves arbitrariness or discrimination or is so fundamental as to undermine a basic public purpose which the guidelines and the statute under which they are issued are intended to achieve."

(Emphasis Supplied)

49. Applying the said principle of laws to the facts of the present case and testing the case of the parties upon touchstone of the law laid down by the courts with respect to the court's insistence of the adherence of the guidelines/ directions and their validity and enforceability, it can be said that the present qualifies all the tests which enable this court to interfere and insist on the due compliance of the guidelines as enforceable one as against permitting the deviations from the same.

50. Having considered the submissions and guidelines of 2012 and other material placed on record, I am of the opinion that the guidelines are bound to be considered at the time of approvals. My reasons for the same are enumerated as under:

Firstly, as seen above, that the existing rules framed under the Drugs and Cosmetics Act do not provide the exhaustive mechanism for the dealing the dealing with the Bio Similar products as there are certain additional aspects which the guidelines insist to be taken into consideration in the process of the grant of the approval in the cases involving similar biologics. The said additional aspects include additional requirements for the clinical trial applications as per CDSCO guidelines which is evident from the reading of the guidelines, additional steps like product characterstization as per clause 6.3.2 of the guidelines, conducting of the quality comparability study as per 6.4 of the guidelines, insistence of the clinical studies and additional data requirements for the studies etc. All these aspects have been specifically provided for the in the guidelines with the preface that the similar biologics are required to be provided with the regulatory pathway keeping in mind the safety, efficacy and quality of a similar biologic to an authorised reference biologic as against the previous pathway which was the abbreviated one. Thus, the existing rules were silent or were not adequate to provide for the pathway for regulating the regime of the control and approval of the bio similar/ similar biologic products in India for the reason of new and latest regime and the

guidelines were therefore framed supplemental to the rules so that the requirements provided therein should be taken into consideration while approving the similar biologics based on the referenced products. Thus, the guidelines were supplemental to the rules framed under the Act and thus cannot be pleaded or stated to be irrelevant or non binding on the office of the defendant No. 1 when the CDSCO is headed by the defendant No. 1 The guidelines of 2012 thus qualify the test that the same are supplemental to the rules and are not aimed to replace or supplant the existing rules.

Secondly, the guidelines of 2012 was aimed at providing the regulatory pathway for the similar biologics in India considering the safety, efficacy and quality of the similar biologic in consideration. Thus, the object sought to be achieved is to ensure the public health and safety so that the pubic should be provided with the medicines that are safe, efficacious and quality wise appropriate and at par with the innovator drugs which are based on artificially engineered micro-organism. Thus, considering the object which was sought to be achieved by the said guidelines which is in consonance with the objects and purposes of Drugs and Cosmetics Act, it cannot be said that the guidelines on similar biologics can be ignored and can be bypassed by defendant No. 1. In the absence of the defendant's complying the same, the outweighing public interests and the purpose sought to achieve by the said guidelines clearly allow this court to interdict in such matter as the deviation from the said guidelines in such a matter would be detrimental to the larger public interest and would be against the objects and reasons of the guidelines which are sought to be achieved at the time of the framing of the same.

Thirdly, it is only the case of the defendant No. 1 and other defendants that by mere fact that the guidelines are not statutory in nature but are issued by CDSCO, therefore the defendant No. 1 despite being participant in framing the guidelines can ignore them (the argument which though I have already rejected separately). None of the defendants have argued or canvassed any submissions that the said guidelines are in contradiction with any rules and regulations framed under the Drugs and Cosmetics Act or ultra vires the Act. In absence any such successful plea of the said contradiction and considering that the guidelines are merely

supplemental to the rules and do not aim to replace the rules but to apply them strictly along with the additional requirements considering the distinct nature of the regime of biosimilar products involved which require greater degree of regulatory measures, it cannot be assumed on a priori basis that the guidelines on similar biologics are empty formality or useless exercise and cannot be implemented by the defendant No. 1. On this ground again, the inference to be drawn is towards the validity and enforceability of the guidelines as against non binding character.

51. It is admitted by the learned ASG that the clinical trials of Phase I and Phase II of the drug in question are not registered with the defendant No. 1, however, the approvals are granted after the justification are given by the defendant No. 3. He submits that as requisite approvals have been granted, thus the plaintiffs are not entitled for an injunction. The suit filed by them is barred by law and is not maintainable and this Court has no jurisdiction to examine the process of approvals which were granted after examining the Rules. The only remedy which was available with the plaintiffs is to file an appeal under Rule 122 BD before the Central Government against the grant of approvals being aggrieved party. The suit filed by them is an abuse of the process of law. However, the stand of the defendant No. 1 again in this matter is also that the guidelines are not statutory in nature. On the other hand, the plea of the defendant No. 3 is that the approvals must have been granted by following the guidelines, though biosimiar Guidelines 2012 may not be applicable. The defendant No. 1 is taking contradictory position before this court when the defendant No. 1 himself is the participant to the framing of the guidelines for the similar biologics, still the defendant No. 1 submits that those are not statutory. If the guidelines are required to be bypassed completely by the defendant No. 1 in practise while granting the approval to the applicants seeking approval on biosimilar, when it is agreed by the defendant No. 1 along with the other relevant persons in the field of the biotechnology that the approvals shall be subject to the guidelines in future, then what is purpose of framing these guidelines at the first place.

52. These guidelines are passed not merely in India but in other countries of the world as well on similar lines so as to create the different pathway to the approval of the drugs which are concerning the bio similar in nature. It is not the clear case

of the defendants No. 1 and 2 that the guidelines are followed but on the contrary it has been argued that the guidelines are not statutory in nature. Thus, the position taken by the defendant No. 1 that the guidelines are not statutory in nature and thus need not be followed is really appalling and creates a compelling circumstance to entertain the present suit as it appears that on face of it that the guidelines for the similar biologics are attempted to be totally bypassed which may prejudicial affect the rights of the plaintiffs as well as other innovators of the drug.

53. Accordingly, I reject the argument of the defendants that the guidelines are of non binding character, not applicable being non-statutory and are thus non enforceable and can be conveniently bypassed by the defendants while granting the approvals for manufacture of medicinal products based on similar biologic. Prima facie I am of the view that bio-similar guidelines of 2012 are applicable and the same are to be considered at the time of grant of approvals of bio-similar product.

Passing Off

54. As far as the common law principle of passing off is pretty clear on the subject for more than 200 years ago when the court of appeal in the case of Frank Reddaway v. George. Barham, (1896) AC 1990 speaking through Lord Hersehell observed on page 209 that if the defendants were entitled to lead purchasers to believe that they were getting the plaintiffs' manufacture when they were not and thus to cheat the plaintiffs of some of their legitimate rights, it would be regretable to find that the law was powerless to enforce the most elementary principles of commercial morality .". The passing off as a principle originally had emerged on the basis of the general statement of law has been developed from time to time and in the modern form includes the use of the signs, trade names, domain names, logos, shape of the products or any indication which allows the consumers to attach the product of the competitor with that of the rival trader in order to deceive them. Thus, the action of passing off is an action in deceit which has been recognised by the Supreme Court of India in case of Laxmikant V. Patel v. Chetanbhat Shah and Another, reported in (2002) 3 SCC 65 : 2002 (24) PTC 1 (SC), wherein the Supreme Court while considering a plea of passing off and grant

of ad interim injunction held in no uncertain terms that a person may sell his goods or deliver his services under a trading name or style which, with the passage of time, may acquire a reputation or goodwill and may become a property to be protected by the Courts. It was held that a competitor initiating sale of goods or services in the same name or by imitating that name causes injury to the business of one who has the property in that name. It was held that honesty and fair play are and ought to be the basic policy in the world of business and when a person adopts or intends to adopt a name which already belongs to someone else, it results in confusion, has the propensity of diverting the customers and clients of someone else to himself and thereby resulting in injury.

55. The passing off is action in deceit. From the observations of Lord Her shell in the case of Redway (supra) at the time of the nascent stage of the evolution of law of passing off, it is clear that the law is not powerless to prevent the most elementary principles of commercial morality and the trading has to be fair and not unfair and in case there is an element of unfairness and deceit to the consumers, the court can always interdict in order to protect the consumer interests and prevent the deceit. Once the Court would notice that the party is trying to make misrepresentation or making a false statement on comparison of two drugs of the parties about the approvals of the product and it may affect the right of the suing party and if the said party alleged that the rival party is trying to disparage the product, the action of passing off would lie. It is immaterial at the initial stage whether any strong case for passing off is made out or not.

56. Even in the case of N. P. Ponnuswami v. The Returning Officer, Namakkal Constituency, Namakkal, Salem Dist. And others, AIR 1952 SC 64, the Supreme Court held as under:-

"12. It is now well-recognised that where a right or liability is created by a statute which gives a special remedy for enforcing it, the remedy provided by that statute only must be availed of. This rule was stated with great clarity by Willes J. in Wolverhampton New Water Works Co. v. Hawkesford, 6 C.B. (N.S.) 336, 356 in the following passage :-

"There are three classes of cases in which a liability may be established founded upon statute. One is where there was a liability existing at common law, and that liability is affirmed by a statute which gives a special and peculiar form of remedy different from the remedy which existed at common law; there, unless the statute contains words which expressly or by necessary implication exclude the common law remedy, the party suing has his election to pursue either that or the statutory remedy. The second class of cases is, where the statute gives the right to sue merely, but provides no particular form of remedy; there, the party can only proceed by action at common law. But there is a third class viz., where a liability not existing at common law is created by a statute which at the same time gives a special and particular remedy for enforcing it..... The remedy provided by the statute must be followed, and it is not competent to the party to pursue the course applicable to cases of the second class. The form given by the statute must be adopted and adhered to."

The rule laid down in this passage was approved by the House of Lords in Neville v. London Express News Paper Limited (1919) A.C. 368 and has been reaffirmed by the Privy Council in Attorney-General of Trinidad and Tobago v. Gordons Grant and Co. (1935) A.C. 532 and Secretary of State v. Mask and Co (1940) 44 C.W.N. 709; and it has also been held to be equally applicable to enforcement of rights : see Hurdutrai v. Official Assignee of Calcutta (1948) 52 C.W.N. 343, 349. That being so, I think it will be a fair inference from the provisions of the Representation of the people Act to state that the Act provides for only one remedy, that remedy being by an election petition to be presented after the election is over, and there is no remedy provided at any intermediate stage."

57. The allegations of the plaintiffs against the defendant No. 3 are that they conducted a very limited clinical trial and cannot be permitted to use the data and information for the plaintiffs' Trastuzumab which is publicly available without independently conducting the tests required under applicable law and without complying with the Drugs Act, the Rules or the Biosimilar Guidelines. They cannot rely upon plaintiffs' data in order to misrepresent TrastuRel as biosimilar to the plaintiffs' Trastuzumab.

58. The plaintiffs submit that the defendant No. 3 has almost reproduced data relating to the plaintiffs' Trastuzumab in the package insert in relation to HER2+ metastatic gastric cancer and HER2+ early breast cancer. The proposed drug of defendant No. 3 i.e. TrastuRel has admittedly not been tested for the HER2+ metastatic gastric cancer and HER2+ metastatic gastric cancer indications.

In part of TrastuRel's package insert, the information required to be described is stated as "reported in literature" or as relating to "trastuzumab" i.e., directing the reader to the plaintiffs' data, without corresponding data relating to TrastuRel, since such data has in fact not been generated for TrastuRel. The package insert for TrastuRel also contains remarks about the plaintiffs' Trastuzumab, particularly in relation to adverse effects. There are positive averments made by the plaintiffs in the plaint about the action of passing off.

59. It is claimed by the plaintiffs that the package insert for the plaintiffs' Trastuzumab is a literary work under the Indian Copyright Act, 1957, as amended (the "Copyright Act") and defendant No. 3 has reproduced the contents of the plaintiffs' package insert in the package insert for TrastuRel amounts to infringement of the plaintiffs' copyright in such package insert.

No doubt the defendant No. 3 is entitled to take the idea and to use the details about the clinical trials independently conducted by them and to compare the same with the plaintiffs drug. However, reproduction of the same would amount to infringement. Defendant No. 3 in the package insert has made a verbatim reproduction of certain content from the plaintiffs' package insert.

The judgment in the matter of Smithkline Beechem Consumer Healthcare, L.P. v. Watson Pharmaceuticals Inc., (United States Court of Appeals, April 4, 2000) relied upon by defendant No. 3 is not applicable to the facts of the present case. The other judgment of District Court (US) cannot be relied upon.

60. The civil right of the plaintiffs being only parting with the innovated product in a regulated regime so that the rival trader can make the biologically similar product for safety, efficacy and another reasons. However, the party should not pass off the defendant's products as those of the plaintiffs.

61. The arguments addressed on behalf of the defendants are not sustainable in view of the decision of the Division Bench in the case of Ganga Ram Hospital Trust v. Municipal Corporation of Delhi, 2001(60) DRJ 549. It was held as under:-

"16. Section 169 provides for a remedy of appeal against levy or assessment of any tax under the Act while section 170 lays down conditions subject to which the right of appeal conferred by section 169 can be exercised. Neither of these two sections contain any provision barring a civil suit to challenge levy and assessment of tax under the Act. At best it may be argued that in view of the remedy of appeal provided under section 169 of the Act a party should have recourse to the said remedy. But a party filing a civil suit to challenge the levy and assessment of tax under the Act may like to urge that the levy and assessment of tax is not in accordance with the Act or is violative of the provisions of the Act. In other words it may be the case of a plaintiff that the authorities under the Act have not acted in accordance with the provisions of the Act while levying and assessing tax and, therefore, it is entitled to exercise its inherent right to challenge such a levy and assessment by way of a civil suit. Availability of an alternative remedy may be treated as a bar by the court while exercising its writ jurisdiction because writ jurisdiction under Article 226 of the Constitution of India is a matter of exercise of discretionary jurisdiction of the court but it is not the same case while entertaining a civil suit. Exercise of jurisdiction to entertain civil suit is not a discretionary matter before the civil court. A civil court may reject the plaint as per law or dismiss a civil suit on merits. It cannot refuse to entertain the suit unless barred by law. The DMC Act does not contain any such bar to a civil suit in matters of levy and assessment of tax."

62. In the case of Norma (India) Ltd. v. Sameer Khandelwal and Ors., reported in 2007(93) DRJ 318, in para 14, it was held as under:-

"14. It is settled law that jurisdiction of the company law board under the Companies Act in relation to Section 397 of the said Act is a concurrent jurisdiction which may be exercised by civil courts where allegations pertaining to oppression and mismanagement partake the character of a civil dispute. Thus, it was the duty of the plaintiff to have made averments in the plaint or in the injunction application,

giving material particulars of the dispute pending before the company law board. In particular, plaintiff ought to have disclosed about CA No. 39/2006 filed under signatures of Shri Gautam Khandelwal."

63. In the case of K.G. Khosla Compressors Ltd. and Ors. v. Khosla Extraktions Ltd. and Ors., 1986 (6) PTC 211 (Del.), this Court in para 31 held as under:

"31. It is not disputed any may it could not be disputed that Civil Courts has jurisdiction in the suit. If any authority is needed reference may be made to decision of this Court in Bhandari Homeopathic Laboratories, (1976) Tax Legal Representative 1382) (supra). The Central Govt. has certainly no power to grant any injunction as prayed for in the present suit though a person disobeying the directions issued under sub-section (1) of Section 22 of the Act might entail punishment. But then in the present suit the plaintiff has also based its cause of action on passing off the name of defendant No. 1 as that of the plaintiff. I would rather say that the jurisdiction of the Central Government under Sections 20 and 22 of the Act and the jurisdiction of the Civil Court operate in two different fields. Further the Central Govt. has to act within the guidelines laid down under Section 20 of the Act, while there are no such limitations on the exercise of jurisdiction by the Civil Court."

64. With regard to the objection raised by the defendants about the exclusivity of civil jurisdiction impliedly bar under Rule 122DC. Rule 122DC does not cover appeals against approvals granted under Part XA - this rule is limited to appeals against orders passed by the DCGI under Part XA of the Rules. The terms "order" and "approval"/ "permission" have distinct meanings under Part XA of the Drugs Rules (refer to Rule 122DAB(3), Rule 122DAB(7), 122DAC(3), 122DAC(4), 122DB and Rule 122B(2A)). In the present suit, the plaintiffs have not challenged any "order" passed by defendant No. 1 under Part XA of the Drugs Rules. It does not confer a right on a third party to challenge an approval granted under Rule 122B Rule 122DC applies to a person who is immediately and directly aggrieved by an order of the licensing authority, inter alia, refusing to grant licence to himself or to renew licence, and not to one who is consequently aggrieved, like the plaintiffs in the present case.

65. No doubt as Rule 122DC contains the appeal provision, the benefit of the appeal would be accrued only to a person who is before the regulator in the first instance and who would, therefore, have the knowledge of the order issued by the regulator. The said party is expected to file an appeal within 60 days from the date of the order, as contemplated under Rule 122DC. In the present case, approval for drug of defendant No. 3 was not made available to the plaintiffs. Accordingly, this provision is not applicable to the plaintiffs in the present case. The approvals of bio-similar in favour of defendant No. 3 of innovator drugs are admittedly never notified of approvals granted or given any information available to manufacturers of innovator drugs. As far as bar of Section 37 of the Act is concerned, as argued by the defendants, there is no force as the suit has not been filed against any Government employee who may have involved in the process of approvals.

66. The said Rule does not protect or enforce the right of the innovator drugs. Even Mr. Sanjay Jain, learned ASG appearing on behalf of the defendants No. 1 and 2, has admitted that the procedure of granting approvals to manufacturers for biosimilar drugs does not involve a lis between the manufacturer of the innovator drug and the manufacturer of the biosimilar drug. Defendant No. 1 does not determine the rights of such parties at the time of granting approvals to drug manufacturers. Therefore, the plaintiffs (i.e. the manufactures of the innovator drug in the present case) are entitled to file a civil suit to protect their rights in relation to the plaintiffs' Trastuzumab as efficacious remedy under this Rule is not available. (See Ganga Ram Hospital v. Municipal Corporation of Delhi, 2001 (60) DRJ 549 at paragraph 20).

67. The arguments of the defendants that a writ petition should be filed to challenge an action under the Drugs Act and the Drugs Rule have also no force as an alternative remedy under a statute may be treated as a bar by the court while exercising its writ jurisdiction because writ jurisdiction under Article 226 of the Constitution of India is discretionary. Writ jurisdiction is not intended as an alternative remedy for reliefs which may be obtained in a suit. An infraction of the State's duty to act in public interest is amenable to examination either in a civil suit or in writ jurisdiction (see Dwarkadas Marfatia and Sons, (1989) 3 SCC 293) at paragraph 21).

68. Even in the judgment of Systopic Laboratories Pvt. Ltd. v. Dr. Prem Gupta and Ors., (1994) Supp (1) SCC 160) referred by the defendants, the writ petitions were not dismissed as non-maintainable on the ground that executive decisions of the expert committee could not be reviewed by courts. As a matter of fact, the Supreme Court reviewed the facts in detail to determine that the matter had been properly examined by the expert committee and did not require judicial interference.

69. It is settled law that Section 34 of the Specific Relief Act is not exhaustive in nature and does not circumscribe the jurisdiction of a court to grant declaratory reliefs in appropriate cases falling outside this provision (See Vemareddi Ramaraghava Reddy v. Kondru Seshu Reddy, AIR 1967 SC 436 and Supreme General Films Exchange Limited v. His Highness Sir Brijnath Singhji and Others, (1975) 2 SCC 530).

70. The decisions in the matters of Delhi Science Forum v. Union of India, (1996) 2 SCC 405), Jasbhai Motibhai Desai v. Roshan Kumar, Haji Bashir and Others, (1976) 1 SCC 671), N.D. Jayal v. Union of India, (2004) 9 SCC 362), NDMC v. Satish Chand, (2003) 10 SCC 38), Rajasthan State Road Transport Corporation v. Bal Mukund Bairwa, (2009) 4 SCC 299) and State of Andhra Pradesh v. M/s. Pioneer Builders, (AIR 2007 SC 113) do not support the defendants' arguments in relation to the maintainability of the present suit. The facts appearing in the present case are entirely different.

71. The present dispute involves complicated questions of fact and evidence, the summary procedure in a purported appeal before the defendant No. 1 or in writ proceedings is not the appropriate remedy. The defendants themselves are admitting that the present dispute is commercial dispute between the two set of parties. As the defendant No. 1 has filed its written statement and has placed its stand before Court and produced the record of approvals of drug of defendant No. 3 before Court, thus, further appearance of defendants No. 1 and 2 in the matter is not necessary, hence the defendants No. 1 and 2 are deleted from the array of the parties. The plaintiffs to file the amended memo of parties within four weeks from today. If so required they are entitled to summon the representative as

witnesse(s).

72. In the light of the above prima facie it appears to the Court that the suit is not barred by law and this Court has also got the jurisdiction to decide the issue involved particularly when the serious allegations are made in the plaint about the approvals granted in favour of defendant No. 3. These issues are required to be decided by the Civil Court who is competent to pass the interim order if the case is made out before Court. Even otherwise when disputed questions of facts are involved, the same have to be determined in civil matter. Prima facie the objections of the defendants are not sustainable and the suit is not barred and the same is maintainable.

73. Now I shall deal with the rival submissions of the parties in relation to main issue involved in the matter i.e. approvals of drug metastatic breast cancer, International Non-proprietary Name (in short INN) Trastuzumab, concept of biosimilar drug and approvals and package insert, extrapolation which are granted by the authorities under the provisions of the Drug Act and Rules.

74. It is necessary to mention the relevant list of details and sequence of events which are mentioned in the written statement of the defendant No. 1 about the stepwise process of approvals conducted by the appropriate authorities. The same are reproduced as under:

DATE	PARTICULARS
23.03.2009	License issued by Joint Commissioner cum License Authority, Govt. of Maharashtra on Form-29 for the purpose of examination, test or analysis.

18.11.2010	RCGM grants permission to conduct pre-clinical toxicological studies to D-3.
28.07.2011	RCGM, based on the pre-clinical toxicological studies, directed D-3 to approach D-1 for conduct of appropriate phase of clinical trial by submitting all relevant information on the entire product development date, including product purification and specifications and pre-clinical toxicity data.
22.02.2012	Letter written by D-3 to the DCGI submitting Form 44 for grant of permission to conduct Phase III clinical trials under Rule 122-DA of the Drugs and Cosmetics Rules, 1945.

23.04.2012	The D-1 seeks information from D-3 regarding the clinical trials.
19.05.2012	Detailed reply given by Reliance for this office query Letter.
25.07.2012	The proposal of Phase III clinical trial of the firm was referred to the NDAC for their opinion.
19.09.2012	The proposal of phase III clinical trial was discussed in the NDAC (Oncology and Hematology)
29.10.2012	On the basis of NDAC recommendation, D-1 granted permission to D-3 to conduct Phase III clinical trials.
30.11.2012	Copies of documents filed by D-3 before the D-1 with regard to notification of amended protocol.

31.12.2012	The D-3 applied for additional site permission. 23.01.2013 Notification of CT protocol version 3.0 dated 13-Dec- 2012.
08.02.2013	Amended permission granted to D-3.
04.03.2013	Protocol amendment permission issued to D-3.
04.03.2013	Additional site permission issued to D-3.
26.04.2013	Notification for the typo error in the CT protocol amendment.
16.05.2013	Notification for revised Informed consent Form.
03.07.2013	Amendment issued for the typo error in the CT protocol amendment.
03.07.2013	Query letter issued for not submitting the Ethics committee approval of the CT protocol.

10.07.2013	Application for inclusion of an additional CT site.
23.07.2013	Approval for inclusion of additional CT site.
23.08.2013	Application for inclusion of 2 additional CT site.
06.09.2013	Follow up for 2 additional sites.
01.10.2013	Application for inclusion of 1 additional CT site.
08.10.2013	Approval for inclusion of 2 additional CT site.
14.10.2013	Application for inclusion of 1 additional CT site.
05.11.2013	Approval for inclusion of 2 additional CT site.
02.01.2014	Submission of interim CT report.
27.01.2014	Notification of annual study report.
29.01.2014	Query letter issued to firm to submit the 10 set of interim report.
06.02.2014	Submission of 10 set of interim report.

11.02.2014	Invitation letter send to SEC members.
04.03.2014	Proposal discussed in the NDAC/SEC meeting on interim report.
27.03.2014 and 15.04.2014	Minutes of TC and Apex Committee wherein Trastuzumab of D-3 was evaluated and recommended for further study.
22.04.2014	Application for inclusion of 3 additional CT site.
07.05.2014	Application for inclusion of 1 additional CT site.
04.06.2014	Approval for inclusion of 4 additional CT site.
27.03.2015	Submission of report of the Phase III studies as conducted by the D-3 to D-1.
05.05.2015	Referred the proposal to SEC (NDAC) for their opinion.

07.05.2015	Phase III clinical trial results discussed in the SEC (Oncology) meeting held on 07.05.2015.
02.06.2015	D-1, after considering all relevant aspects, granted permission to D-3 to manufacture TrastuRel on Form 46 and 46A for bulk.
15.09.2015	28 D License received from SLA for CLAA approval.
21.10.2015	D-3 submitted the specimen copy of labels, carton and package insert for review and approval.
27.10.2015	SEC deliberated the package insert and suggested modification in the same.
02.11.2015	D-1 communicated the firm to submit the revised package insert for approval.
03.11.2015	Firm submitted the revised package insert for approval.

07.12.2015	Approval for package insert granted by this office.

75. It is submitted by the plaintiffs that in India, a biosimilar is usually approved with the corresponding INN of the innovator reference product. The practise of approving and marketing biosimilars under the INN of the innovator biological drug is not in accordance of the recommendations of the World Health Organisation regarding use of INNs by biosimilar manufacturers. Such recommendations acknowledge the necessity to distinguish a similar biologic from the innovator biological drug by use of unique biological qualifiers by the biosimilar manufacturers. It is an established biosimilar drug (approved as such after adequate testing under applicable law) may be entitled to use the INN assigned to the innovator biological drug. No biosimilar drug manufacturer is entitled to use the INN without conducting necessary tests and establishing biosimilarity under applicable law. In the absence of such tests, the defendant's drug cannot be approved as 'Trastuzumab' and cannot be marketed as such.
76. The main case of the plaintiffs is that the defendant No. 3 has not conducted various tests required under applicable law for the approval of the drug. Phase I and Phase II trials have also not been registered with the defendant No. 1. The comprehensive details to challenge the approvals are already mentioned in para 21 of my order. The defendant No. 3 has also not independently generated requisite data in order to demonstrate similarity between the drug and the plaintiffs' Trastuzumab, both in terms of the stages and the sample size of the tests conducted by defendant No. 3.

77. Counsel for the plaintiffs has also relied upon the averments made in the plaint wherein it is mentioned that the drug of the defendant No. 3 for which approval was granted is not biosimilar on various reasons and there is an inadequacy of TrastuRel's approvals of HER2+metastatic breast cancer. Defendant No. 3 has failed to establish the biosimilarity of its drug TrastuRel with the plaintiffs' Trastuzumab who also did not do product characterisation studies with the plaintiffs' Trastuzumab as required under Clauses 6,3.2, 6.3.3, 6.3.4 and 6.4 of the

Biosimilar Guidelines. The allegation of the plaintiffs is that only stand-alone tests seem to have been conducted, which are not sufficient to establish similarity between the plaintiffs Trastuzumab and TrastuRel. In the absence of 'head to head' comparison at the product characterisation stage, TrastuRel cannot be approved by defendant No. 1 as a biosimilar version of the plaintiffs' Trastuzumab. With regard to pre-clinical studies, defendant No. 3 did not conduct animal pharmacology tests in relation to TrastuRel as part of its pre-clinical studies, in violation of the provisions of paragraph 1(1) (ii) of Schedule Y, item 3 of Appendix 1 read with Appendix III and IV of Schedule of the Drugs Rules and Clause 7.2 of the Biosimilar Guidelines, as reflected in defendant No. 3's letters dated January 4, 2010, July 12, 2010 and May 4, 2011 and defendant No. 1's letter dated November 18, 2011.

It is also alleged that the defendant No. 3 has also not conducted a study of immune responses (immunogenicity) in animals in relation to TrastuRel prior to using TrastuRel in human clinical trials. Immunogenicity studies are essential and mandatory under paragraph 1.6 of the Guidelines for Generating Pre-clinical and Clinical data for RDNA Vaccines, Diagnostics and Other Biologicals, 1999, read with item 2.5 of Appendix I of Schedule Y of the Drugs Rules and Clause 7.3 of the Biosimilar Guidelines. The letter dated 12th July, 2010 sent by the defendant No. 3 to defendant No. 1 would show that defendant No. 3 has also not conducted comparative pre-clinical studies with the plaintiffs' Trastuzumab as required under Clause 7 of the Biosimilar Guidelines. In the absence of comparative pre-clinical studies, TrastuRel cannot be approved by defendant No. 1 as a biosimilar version of the plaintiffs' Trastuzumab.

78. On the other hand, it is stated by the defendant No. 3 that though the clinical trials of Phase I and Phase II have not been registered with the defendant No. 1 but it did not skip Phase I trial as the main the objective of a Phase I trial is to establish comparative pharmacokinetics (pK) and this pK data was generated by defendant No. 3 as the initial part of the Phase III trial. Defendant No. 3 did the Phase I and Phase II trials as part of the same sequential study since it was necessary to do the pK study in patients and not in healthy volunteers. The phase III studies were also registered with the Clinical Trial Registry-India ('CTRI'). The

2012 Guidelines also contemplate that PD study can also be a part of Phase III clinical trials.

Defendant No. 3 gave its justification for not doing the Phase II study as dose finding and POC studies are not required for follow-on products (biosimilars or generics) and this justification was accepted by the defendant No. 1.

79. In reply to submission made by the plaintiffs, learned counsel for the defendant No. 3 has made her submission by referred the Rules and Schedule 'Y', the defendant No. 3 made the following submissions:

(i) Trastuzumab is a drug which has already been approved in India. The plaintiff itself was granted permission under Rule 122 A of the Drugs and Cosmetics Rules to import and market the product Trastuzumab powder for Injection on 11th October, 2002.

(ii) The defendant No. 3 product was granted the permission to manufacture the drug for the purpose of test and analysis. Subsequent to manufacture of the drug for the purpose of test and analysis, the RCGM has granted the permission to the defendant No. 3 for pre clinical and toxicological studies of the drug trastuzumab. Thereafter, the RCGM based on the review of completion of the pre clinical and toxicological study report granted the permission to the defendant to approach the answering defendant for conduct of appropriate phase of clinical trial. Thereafter the defendant No. 3 approached the answering defendant along with Form 44 for grant of permission to conduct Phase III clinical trial. The application for the conduct of Phase III clinical trial was examined and approved by the Subject Expert Committee of Oncology, Technical Committee and Apex Committee. Thereafter the defendant No. 3 submitted the report of the Phase III clinical trial for obtaining the grant of permission for manufacture of trastuzumab.

(iii) In view of the above, the entry B of Form 44 is applicable to the defendant No. 3's application to manufacture the drug in question. In terms thereof, any application of defendant No. 3 is to be accompanied by requisite fee and such information and data as required by Appendix 1 or Appendix IA of Schedule Y.

(iv) Schedule Y does not make it mandatory for conducting phase 1 and phase 2-clinical trials for drugs which have already been approved in India and even for drugs approved outside India. Instead, appendix lA specifies the "Data required to be submitted by an application for grant of permission to import and/or manufacture a new drug already approved in the country". Further, Schedule Y also prescribes that "for new drugs approved outside India, phase III studies need to be carried out primarily to generate evidence of efficacy and safety of the drug in Indian patience when used as recommended in the prescribing information.

(v) Schedule Y does not specify number of the subjects to be enrolled in different phases of clinical trials. It however, provides a general provision indicating that the number of subjects will depend upon the nature and objective of the study. However, as per GCP guidelines, no of subjects in various stages of clinical trial are as under:-

Phase I - At least two subjects should be used in each dose.

Phase II - Normally 10-12 patients should be studied at each dose level. These studies are usually limited to 3-4 centres.

Phase III - If the drug is already approved / marketed in other countries, phase III data should generally be obtained on at least 100 patients distributed over 3-4 centre primarily to confirm the efficacy and safety of the drug, in Indian patients when used as recommended in the product monograph for the claims made.

80. It is argued by the counsel that the data is required to be submitted by an applicant for grant of permission to import and / or manufacture a new drug already approved in the country, as specified in appendix IA of Schedule Y to Drugs and Cosmetics Rules, includes chemical and pharmaceuticals information including structure physicochemical properties, dosage form, its composition, test specification method of manufacture etc., stability data, sub-acute animal toxicity data for I.V. Infusion and inject ables. Therefore, the challenge of the plaintiffs towards approvals is baseless as alleged by the learned Senior counsel for the defendant No. 3 who stated that all the requisite clinical trials have been conducted and whenever are the exempted under the Guidelines 2012, the

discretion is exercised in favour of defendant No. 3 as well as under the Act and Rules.

81. The defendant No. 3 submits that the comparability was established by way of lab testing in a head-to-head manner and the results were submitted to the IBSC, RCGM. Data establishing the product characterisation as well as the preclinical studies protocol was presented before the relevant authority.

(i) The Defendant No. 3 has conducted the studies which include physicochemical properties, biological activity, immunological properties, functional assays, purity (process and product-related impurities etc.), contamination, strength, and content.

(ii) Further the Defendant No. 3 has also performed an extensive physicochemical, biochemical and biological characterisation on Defendant No. 3's Product "TrastuRel".

(iii) It is submitted that details of characterisation and comparability assessment establishing TrastuRel's biosimilarity to the innovator Trastuzumab were detailed in dossiers submitted by the Defendant No. 3 to RCGM and DCGI.

82. The defendant No. 3 further stated that the biosimilarity assessment includes biological, functional and safety evaluation of any differences observed between the two products and is consistent with Biosimilar guidelines of 2012. The Critical Quality Attributes (CQAs) for TrastuRel have been assigned based on consideration of safety, potency, efficacy and molecular mechanism of action. Overall, the assessment of critical quality attributes demonstrates a high level of comparability with the innovator Trastuzumab. The dossier submitted had the complete details of:-

a) Product characterisation.

b) Pre-clinical study protocol.

The said dossier was duly evaluated by the RCGM in detail and suggestions were given and defendant No. 3 was asked to give revised dossier. Revised Dossier was duly filed by defendant No. 3 and has complied with requirements.

Comprehensive lab testing and animal testing was done. The revised dossier was submitted in July 2010 and after 4 months, the RCGM issued permission to the defendant No. 3 to carry out pre-clinical toxicology studies on Trastuzumab monoclonal antibody.

As per Biosimilar Guidelines 2012, in-vivo pharmacodynamics tests may be dispensable if in vitro pharmacodynamics assays are available. The said data of the in vitro assay was submitted by the defendant No. 3 to RCGM for their review and same was approved by the RCGM.

83. As per Schedule Y (2)(8)(iii), PK studies can be conducted along with Phase III clinical trials. The New Drug Advisory Committee (NDAC), Technical Committee, Apex Committee and DCGI approved the Phase III study and recommended that the pharmacokinetic (PK) part of the study be conducted first and the same be submitted to the Data Safety Monitoring Board (DSMB) and CDSCO for approval, and only then, the rest of the Phase III study be continued on the same participating patients. No 'separate pharmacokinetic tests' were recommended. The defendant No. 3 submitted the Interim Study Report to the DSMB for Pharmacokinetic studies that were conducted as part of Phase III studies. Hence, defendant No. 3 initiated the Phase III study with the PK portion of the study in 42 patients and, after receiving approval of the results of the PK portion from the DSMB and DCGI, went ahead with the rest of the Phase III study in the same patients and additional patients adding up to a total number of 105 as suggested by the NDAC and DCGI.

84. Schedule Y completely exempts conduct of Phase I trials and only data from other countries, needs to be submitted as per Entry 5 of Appendix 1. As per the NDAC recommendation dated 19th September, 2012, the PK part of the study was to be conducted based on DSMB reports, and the second part of the study proposed by the defendant No. 3 could have been continued on the same subjects included in the PK study.

After completion of the comparative animal toxicity studies and based on RCGM recommendation, the defendant No. 3's comparative Phase-III Clinical Trial was designed to compare the defendant No. 3's biosimilar version of Trantuzumab and

the Inventor's Trastuzumab in terms of PK (Primary End Point) and efficacy as secondary end point. The trial also assessed safety including Immunogenicity of defendant No. 3's drug and compared it with reference biological product of the Inventor before submitting the same to CDSCO for evaluation.

85. Even as per Guidelines on Similar Biologics, it is not mandated to conduct Phase II clinical trials. The same is reiterated in the WHO guidelines. The indications and dosage of Trastuzumab in the approved indications have already been well established. Thus there is no requirement to have proof of concept study for Trastuzumab either to identify suitable disease indications or suitable dose in subjects suffering from any of the approved indications. The dosage of Trastuzumab in the approved indications is already well established. The same approved dosage was to be applied in the Phase III trial by the defendant No. 3.

Phase III clinical trials were conducted in accordance with the Clinical Trial Protocol Version 3.0 as was approved by the DCGI on 4th March, 2013. As per the Biosimilar guidelines, Pharmacokinetic studies may be conducted in patients. This is also accepted worldwide. Since the NDAC and DCGI advised the defendant No. 3 to conduct the PK study as part of the Phase III clinical trial, the defendant No. 3 complied with this requirement. Safety is a standard secondary endpoint of Phase III trials. It was studied in the Phase III trial on TrastuRel through monitoring of adverse events, changes in laboratory parameters, vital signs and immunogenicity.

86. The defendant No. 3 presented their report on their clinical trials before the 27th SEC (Oncology) meeting held on 7th May, 2015. The report was presented before SEC and DCGI members and detailed the modules submitted to the DCGI on 27th March, 2015 as well. The clinical trial/study report was evaluated by the 27th SEC (Oncology) in the meeting held on 7th May, 2015. The SEC recommended the grant of marketing authorisation of Trastuzumab injection for the three indications applied for by the defendant No. 3.

87. In any event the defendant No. 3 has done Pharmacodynamic studies and Dosage studies as part of the Phase III wherein it has compared TrastuRel with plaintiffs' products. In a biosimilar all that is required to be done is establishing

similarity for the purposes of safety and efficacy. If the product applied is similar in the same dosage, then it has to exhibit the similar properties as to safety and efficacy.

88. The exemptions given are qua the drug in question irrespective of the applicant. Rule 122B (3) of the Drug Rules when using the words "in the name of the applicant" qualifies it with "by the licensing authority mentioned in Rule 21". Even the plaintiffs have no approval by Central Government which is the authority under Rule 21.

The words "the drug" relate to Trastuzumab irrespective of the person manufacturing it. If Trastuzumab is approved in another country and data is available, then reliance can be placed upon the same by a subsequent applicant.

Either both parties can rely on the data from other countries or both cannot.

89. It is denied by the defendant that all phases including local trials have to be conducted in Phases I, II and III sequentially. Only thereafter results have to be compared. This argument is neither borne out from the Act or the Rules or the Guidelines. If Phase I, II and III is done without comparison and then comparison is done on the basis of data generated in Phase I, II and III, the same would not be a head-to-head comparison as is needed.

90. With regard to objection raised by the plaintiffs that Manufacturing No Objection Certificate was not obtained, it is submitted that Manufacturing NOC application to the defendant No. 1 (DCGI) was not filed initially during 2009 for initiating RandD work. During that period, manufacturers used to get the Form 29 directly from State FDA. Please note that the Gazette notification about r-DNA derived drugs being covered under "New Drugs" came into effect only from 24 Jan 2011. Subsequent to that Gazette notification, all manufacturers were expected to approach the DCGI for Manufacturing NOC for initiating RandD of r-DNA products. As the defendant No. 3 applied for the manufacturing NOC prior to the said notification, the defendant No. 3 did not approach the DCGI for the Manufacturing NOC and instead, approached State FDA directly for issuance of Form 29 in 2009. The defendant No. 3 filed for Manufacturing NOC to manufacture R andD batches

in December 2014.

91. Counsel appearing on behalf of the defendant No. 3 submitted that the defendant No. 3 has complied all the steps as mentioned in para 25 of the plaint who has also complied the Bio-similar Guidelines 2012, the Drugs and Cosmetics Act, 1940 and Drugs and Cosmetics Rules, 1945.

92. The details of justification have been provided for not performing pharmacodynamics (PD) study for Trasturel. The details of justification for extrapolation of safety and efficacy data from one indication of Trastuzumab to the additional indications are also given in the reply. The defendant No. 3 has also given the chart by analysis of Appendix I showing fulfilment of all requirements. The comparative analysis of different jurisdiction for abbreviated pathways on bio-similar is filed along with status of data exclusively in different countries of the world.

93. Number of other submissions of defendant No. 3 and Defendants No. 1 and 2 are common. Learned Senior counsel appearing on behalf of the defendant No. 3 has referred a large number of documents in order to establish that due process has been followed and there is no lapse on the part of the defendant No. 1 and any other authority while granting the approval in favour of his client.

94. The defendant No. 3 admits that it has not performed a Pharmacodynamics (PD) study for TrastuRel neither as a separate study nor as a part of the Phase III study. It is the study of the biochemical and physiological effects of drugs on the body and the mechanisms of drug action and the relationship between drug concentration and effect. The justification given by the defendant No. 3 is that Pharmacodynamics (PD) study not required for Trastuzumab because of inter-individual (inter-patient) variability in antibody pharmacodynamics as antibodies such as rituximab, cetuximab, and trastuzumab are designed to bind to proteins on the cell's surface to mediate the destruction of target cells. Antibodies may eliminate cells by blocking or cross-linking cellular receptors and inducing cell death, or by "effector functions" of the immune system.

It is stated that if there are variations in the expression of the target cells or in the expression of receptors associated with effector pathways, one can expect that there will be inter-individual (inter patient) variability in antibody pharmacodynamics. Due to the variability of the pharmacodynamics in human, it is difficult to study it and specifically attribute changes to the drug being tested. The said Pharmacodynamic parameter for Trastuzumab is not well-established as it is a complexity of measuring the response in the form of a change in HER2 receptor expression and inherited variability in pharmacodynamic response to Trastuzumab in the treatment of breast cancer due to polymorphism of HER-2 proto-oncogene.

95. Counsel for the defendant No. 3 has also informed that in many countries of the world have followed the procedure of biosimilar pathways and data and/or marketing exclusivity for innovator biologics and as details available in public domain and as pathway in place as of today. It is stated that thus it is clear that biosimilar abbreviated pathways would/can be adopted in India in which there is condition available as of today pertaining to Data Exclusivity for a reference product. The details would show that no doubt in many countries in the world as per Government policy biosimilar abbreviated pathways exit and in some of the countries right of data exclusivity is granted but in many countries said exclusivity is not granted. Learned counsel appearing on behalf of both parties have informed that so far Government has not taken any conclusive decision or framed any policy as to whether data exclusivity should be given or not. The said issue is being discussed on higher level in this country and other part of the world. However, till the time any policy decision is taken, the Court has to proceed with the matter as per existed law applicable to the case.

96. Let me deal with the rival submissions of the parties as per material available on record.

97. In view of the nature of disputes, it is necessary to examine as to (i) whether the procedure as per rules has been followed or not at the time of grant of approvals of the bio-similar drug to defendant No. 3; (ii) whether the clinical trials of Phase I and Phase II are necessary for the purpose of granting the approval of drug to a biosimilar drug; (iii) whether any Phase can be exempted or any phase

can be combined with subsequent Phase if biological drugs/ bio-similar product is involved; (iv) whether the Guidelines of 2012 are to be followed by the Authority; (v) whether the defendant No. 1 has followed the due procedure prescribed under the Drug and Cosmetics Act, 1940 (as amended) at the time of granting approvals in favour of defendant No. 3; (vi) If granted whether the same are granted by lapsing the procedure and due process, what are the consequences of inadequacy of details.

98. Before dealing with the submissions, it is necessary to mention that it is admitted in the written statements that in the Act and Rules the term "Similar Biologics" has not been defined. The defendant No. 3 neither applied for permission to conduct Phase I and Phase II clinical trials nor those were registered with the defendant No. 1.

99. It is a well-settled salutary principle that if a statute provides for a thing to be done in a particular manner, then it has to be done in that manner and in no other manner. (See Nazir Ahmad v. King Emperor, AIR 1936 PC 253(2); Rao Shiv Bahadur Singh v. State of Vindhya Pradesh, AIR 1954 Supreme Court 322; State of Uttar Pradesh v. Singara, AIR 1964 SC 358). When the State lays down the Rules, the same are imperative to be followed.

100. The defendant No. 1 in its written statement has admitted that the clinical trials of Phase I and II are not registered with the authority but only the trial of Phase III has been registered with the defendant No. 1. On the other hand, the stand of the defendant No. 3 is that the clinical trial of Phase I is combined with Phase III and Phase II trial was skipped in accordance with law.

101. It is not disputed by any of the parties that biological drugs are synthesised by cells of living organisms, as opposed to chemical drugs which are produced by chemical synthesis. 'Biosimilars' are biological drugs that are similar to the innovator biological drug. Due to Owing to the complexity in the molecular arrangement and manufacturing process of a biological drug, it is not possible to replicate the structure and steps involved in the manufacture of the innovator biological drug and to produce an identical follow-on biological drug. Biosimilars, therefore, cannot be generic equivalents of the innovator biological drug. The

generic drugs are characterised by their chemical and therapeutic equivalence to the original, low molecular weight chemical drugs. These are identical to the original product and are sold under the same chemical name.

102. The plaintiffs in their Annual Reports have acknowledged the existence of biosimilars if the same may be safe and efficacious alternatives to the innovator drug. They have also stated that the WHO Guidelines on SBP's should be followed by all countries for the development of their regulatory framework for biosimilars in order to ensure safety and efficacy of a biosimilar product. The relevant extracts from the plaintiff's Annual Reports have supported the development for the approval of biosimilar products it is granted as per law applicable to the regulatory authorities by following the WHO guidelines on evaluation of similar biotherapeutic products.

103. The defendants admit that the procedure laid down in the Act and Rules are to be applied stringently. Even this Court has the same view that all the protocol of biosimilars must be adhered to all the compliance by demonstrating to the regulatory authorities a high degree of structural and functional similarity between their products and the approved original product.

The party, who applies for any approval, must satisfy the authorities that biosimilar manufacturing and marketing process is well understood as biosimilar is a biological product that is almost and highly similar except minor meaningful differences from the approved biological drug in terms of safety, priority and potency otherwise it would lose its meaning.

104. Let me first discuss that the approval process for generic drugs is not the same as the approval process for biosimilars. Biological drugs are synthesised by cells of living organisms, as opposed to chemical drugs which are produced by chemical synthesis. The 'Biosimilars' are biological drugs that are similar to the innovator biological drug. It is admitted by all parties that it is not possible to replicate the structure and steps involved in the manufacture of the innovator biological drug and to produce an identical follow-on biological drug. Thus, biosimilars cannot be generic equivalents of the innovator biological drug.

The generic drugs are characterised by their chemical and therapeutic equivalence to the original, low molecular weight chemical drugs. These are identical to the original product and are sold under the same chemical name.

Distinction between bio-similar and generic drugs.

105. The Generic drugs are approved by testing procedures as two drugs i.e. the applicant and innovator are identical of chemical compound which cannot be applied to biosimilars. As it is associated with the long term safety, efficacy and immunogenicity of biosimilars are significantly higher when compared to those associated with a generic drug.

106. The procedure for approval to manufacture a generic drug for sale and distribution under the Drugs and Cosmetics Act, 1940, as amended (the "Drugs Act") and the Drugs and Cosmetics Rules, 1945, as amended (the "Drugs Rules") is given as under:

a) Under Explanation (ii) of Rule 122E of the Drugs Rules, generic drugs would fall under two categories (I) generics of chemical drugs which have been in the market for more than 4 years and are therefore not 'new drugs' under Rule 122E of the Drugs Rules; and (II) generics of chemical drugs which have been in the market for less than 4 years and are therefore 'new drugs' under Rule 122E of the Drugs Rules.

b) In case of generics of chemical drugs which have been in the market for more than 4 years, the procedure for approval to manufacture the generic drug for sale and distribution is under Part VII of the Drugs Rules which is as follows:

(i) The application for licence to manufacture is required to be made under Rule 69 of the Drugs Rules to the State FDA under Form 24.

(ii) The licence for such manufacture is subsequently granted by the State FDA in Form 25 under Rules 70 and 71 of the Drugs Rules.

(iii) This procedure is similar to the procedure for obtaining manufacturing licence for r-DNA drugs from the State FDA under Rules 75 and 76 of the Drugs Rules in

Form 28D.

(iv) However, unlike in the case of approval for 'new drugs' under Part XA, no approval from Defendant No. 1 is required under Part VII of the Drugs Rules prior to obtaining the State FDA licence.

107. The generics of chemical drugs which have not been in the market for more than 4 years are considered 'new drugs' under Explanation (ii) of Rule 122E of the Drugs Rules. The procedure for approval to manufacture such generic drugs for sale and distribution is under Part XA of the Drugs Rules. In case of generics of chemical drugs which have been in the market for less than 4 years, the generic 'new drugs' can either be generic versions of chemical drugs already approved in India or otherwise.

108. For approval of generic versions of chemical drugs not approved in India, the application for manufacturing authorisation has to be made under Rule 122B of the Drugs Rules in Form 44 and has to be accompanied by data in Appendix I to Schedule Y of the Drugs Rules, whereas, for approval of generic versions of chemical drugs already approved in India, an application under Rule 122B of the Drugs Rules in Form 44 has to be accompanied by data in Appendix IA to Schedule Y of the Drugs Rules. Appendix IA is applicable only to generics and not biosimilars as it requires the submission of bioavailability/bioequivalence data to defendant No. 1.

109. The defendants' drug is a Recombinant DNA (r-DNA) derived drug. Under Rule 122E of the Drugs Rules, all r-DNA derived drugs are treated as "new drugs" as being biosimilar, hence the defendants' drug, which is a "new drug" under Rule 122E. The defendants No. 1 and 3 have admitted that drug of defendant No. 3 developed indigenously and tests were not conducted by the defendant No. 3 globally which has also not been approved in any country outside India. The approval granted on 2nd June, 2015 is the first time approval of manufacturing.

110. Biosimilar drugs are 'new drugs' under Explanation (i) of Rule 122E of the Drugs Rules, and therefore, the entire pre-clinical and clinical data is required to be submitted for their approval. Under Rule 122B(1)(b) and 122B(2) of the Drugs

Rules, the application for such approval has to be made to defendant No. 1 in Form 44 of the Drugs Rules along with the data in Appendix I.

111. The issue in hand admittedly does not pertain to bioequivalence. It is in fact in relation to bio-similarity.

112. Under paragraph 3(5) of Schedule Y of the Drugs Rules, bioequivalence and bioavailability studies are to be conducted in accordance with the Guidelines for Bioavailability and Bioequivalence Studies (March 2005) (the "Bioequivalence Guidelines"), which reflect that such studies are applicable only to generic drugs, and not biosimilars, for the purpose of their comparison with the reference chemical entity. The Bioequivalence Guidelines state that:

Bioequivalence studies are conducted for comparison of two medicinal products containing the same active ingredient.

The two drugs should be therapeutically equivalent (containing the same active substance and clinically showing the same efficacy and safety) in order to be considered interchangeable.

The Bioequivalence Guidelines deal with studies for a generic drug.

113. This Court in Bayer Corporation and another v. Union of India and Others, (2010 (43) PTC 12 (Del) (DB)) has rightly held that Appendix IA to Schedule Y of the Drugs Rules applies to generic versions of a patented drug. The manufacturer of a generic version of a patented drug is only required to satisfy defendant No. 1 that its drug is bioavailable and bioequivalent to the patented drug (as required under Appendix IA). Even phase III clinical trials are not required for generics under Appendix IA.

Defendant No. 3 in the present case has admitted that its application in Form 44 was accompanied with data in Appendix I to Schedule Y of the Drugs Rules and not under Appendix IA.

114. A biosimilar drug is not considered the same as the approved reference product and the procedure applied for the approval of "new drugs already

approved" in India or abroad, which is applied in the case of generics (i.e., chemical drugs), cannot be applied to biosimilars.

115. The definition of "new drug" has been specified in Rule 122E of Drugs and Cosmetics Rules while the requirements and guidelines for permission to Import and/or Manufacture of new drugs for sale or to undertake clinical trials are specified in Rules 122A, 122B, 122D and Schedule-Y of the Rules. Rule 122E of the Rules reads as under:

"Rule 122E - Definition of new drugs

(a) A drug, as defined in the Act including bulk drug substance which has not been used in the country to any significant extent under the conditions prescribed, recommended or suggested in the labelling thereof and has not been recognised as effective and safe by the licensing authority mentioned under rule 21 for the proposed claims:

Provided that the limited use, if any, has been with the permission of the licensing authority.

(b) A drug already approved by the Licensing Authority mentioned in Rule 21 for certain claims, which is now proposed to be marketed with modified or new claims, namely, indications, dosage, dosage form (including sustained release dosage form) and route of administration.

(c) A fixed dose combination of two or more drugs, individually approved earlier for certain claims, which are now proposed to be combined for the first time in a fixed ratio, or if the ratio of ingredients in an already marketed combination is proposed to be changed, with certain claims, viz indications, dosage, dosage form (including sustained release dosage form) and route of administration. (See items (b) and (c) of 3[Appendix VI] to Schedule Y.)

Explanation - For the purpose of this rule-

(i) all vaccines and recombinant DNA (r-DNA) derived drugs shall be new drugs unless certified otherwise by the Licensing Authority under Rule 21;

(ii) a new drug shall continue to be considered as new drug for a period of four years from the date of its first approval."

116. As far as studies and clinical trials examined by expert committees and approvals thereon are concerned, at this interim stage, the Court does not wish to express any opinion or to make comments thereon. However, it is admitted position that the defendant No. 3 in the present matter had refused to give the inspection of said relevant record to the plaintiffs rather the defendant No. 3 has filed the application who claimed confidentiality of the those documents.

117. Defendant No. 3 has argued that as per Indian law and certain other jurisdictions provide for purportedly abbreviated pathways for follow-on biologics, pursuant to which the requirement to conduct all stages of tests and studies for the approval of biosimilar drugs is waived simply by virtue of the innovator drug having conducted all such studies and tests (including all phases of clinical trials), as applicable.

118. Defendant No. 3 has relied upon the first proviso to Rule 122B (3) of the Drugs Rules to contend that local clinical trials for the drug were exempted on the basis of data available from other countries. Defendant No. 3 also seeks to rely upon the second proviso to Rule 122B (3) under which reduction of trial data may be permitted for "new drugs approved and marketed for several years in other countries". Admittedly, the drug has not been approved and marketed in any country outside India.

119. It is also argued on behalf of the defendant No. 1 stating that from a conjoint reading of the relevant Rules and Schedule 'Y', it emerges that Trastuzumab is a drug which has already been approved in India as the plaintiffs themselves were granted permission under Rule 122 A of the Drugs and Cosmetics Rules to import and market the product Trastuzumab powder for Injection on 11th October, 2002. In view of the above, the second proviso to Rule 122A (1) (b) is applicable to the defendant No. 3's application to manufacture the drug in question. In terms thereof, any application of defendant No. 3 is to be accompanied by requisite fee and such information and data as required by appendix I or appendix IA of schedule Y which does not make it mandatory for conducting phase 1 and phase 2

clinical trials for drugs which have already been approved in India and even for drugs approved outside India. Instead, appendix IA specifies the "Data required to be submitted by an application for grant of permission to import and/or manufacture a new drug already approved in the country". Further, schedule Y also prescribes that "for new drugs approved outside India, phase III studies need to be carried out primarily to generate evidence of efficacy and safety of the drug in Indian patience when used as recommended in the prescribing information". Schedule Y does not specify number of the subjects to be enrolled in different phases of clinical trials. The data required to be submitted by an applicant for grant of permission to import and / or manufacture a new drug already approved in the country, as specified in appendix IA of Schedule Y to Drugs and Cosmetics Rules, includes chemical and pharmaceuticals information including structure physical, chemical properties, dosage form its composition, test specification method of manufacture etc., stability data, sub-acute animal toxicity data for I.V. Infusion and inject ables.

120. Defendant No. 1 has further explained that it applied Rule 122A (relating to permission to import new drugs) and Rule 122D (relating to permission to import or manufacture fixed dose combination) of the Drugs Rules, which are irrelevant in case of the defendants' drug.

121. It is submitted by Mr. Sanjay Jain, learned ASG on behalf of defendant No. 1, that even otherwise paragraph 1(3) of Schedule Y of the Drugs Rules relates to abbreviated toxicological and clinical data requirement for drugs indicated for serious and life threatening diseases and is applicable to the approval of defendant No. 3. As the defendant No. 3's application related to a drug already approved in India, the DCGI reviewed the application under Appendix lA to Schedule Y of the Rules.

122. It is admitted by the defendant No. 1 that on 27th March, 2015 the defendant No. 3 applied to defendant No. 1 in Form-44 for approval to manufacture and market the under Appendix of Schedule Y of Rules. There is nothing on record produced before Court by the defendant No. 1 which would show that it has exercised its discretion in writing to abbreviate the clinical trials of Phase I and

Phase II or any other clinical trial(s) under sub-rule 3 of Rule 1 of the Schedule Y of the Drug Rules.

123. In order to understand on this aspect, it is necessary to examine Rule 122B as well as para1(I)(iv)(b) of Schedule Y wherein an application is to be filed for permission to import manufacture new drugs for sale or to understand clinical trials. The said application has to be made in Form-44 accompanying with data in accordance with Appendixes.

124. Para 1(1) (iv)(a) and (b) of Schedule Y reads as under:

"Para 1(1) (iv) of Schedule Y - human Clinical Pharmacology Data as prescribed in Items 5, 6 and 7 of Appendix I and as stated below:-

(a) for new drug substances discovered in India, clinical trials are required to be carried out in India right from Phase I and data should be submitted as required under Items 1, 2, 3, 4, 5 (data, if any, from other countries) and 9 of Appendix I;

(b) for new drug substances discovered in countries other than India, Phase I data as required under Items 1, 2, 3, 4, 5 (data from other countries) and 9 of Appendix I should be submitted along with the application. After submission of Phase I data generated outside India to the Licensing Authority, permission may be granted to repeat Phase I trials and/or to conduct Phase II trials and subsequently Phase III trials concurrently with other global trials for that drug. Phase III trials are required to be conducted in India before permission to market the drug in India is granted;"

125. In order to understand the scheme of Rule 122B, the same is reproduced as under:

Rule 122B Application for approval to manufacture new drug -

"(1)(a) No new drug shall be manufactured for sale unless it is approved by the Licensing Authority as defined in clause (b) of rule 21

(b) An application for the grant of approval to manufacture the new drug and its formulations shall be made in Form 44 to the Licensing Authority as defined in clause (b) of Rule 21 and shall be accompanied by a fee of fifty thousand rupees:

Provided that where the application is for permission to import a new drug (bulk drug substance) and grant of approval to manufacture its formulation/s, the fee to accompany such application shall be fifty thousand rupees only.

Provided further that where a subsequent application by the same applicant for that drug, whether in modified dosage form or with the new claims, is made, the fee to accompany such subsequent application shall be fifteen thousand rupees:

Provided also that any application received after one year of the grant of approval for the manufacture for sale of the new drug, shall be accompanied by a fee of fifteen thousand rupees and such information and data as required by Appendix 1 or Appendix 1-A of Schedule Y, as the case may be.

(2) The manufacturer of a new drug under sub-rule (I) when applying for approval to the Licensing Authority mentioned in the said sub-rule, shall submit data as given in Appendix 1 to Schedule Y including the results of clinical trials carried out in the country in accordance with the guideline specified in Schedule Y and submit the report of such clinical trials in the same format given in Appendix II to the said Schedule.

(2A) The Licensing authority as defined in clause (b) of rule 21 after being satisfied that the drug if approved to be manufactured as raw material (bulk drug substance) or as finished formulation shall be effective and safe for use in the country, shall issue approval in Form 46 and/or Form 46A, as the case may be, subject to the conditions stated therein:

Provided that the Licensing Authority shall, where the data provided or generated on the drug is inadequate, intimate the applicant in writing, and the conditions, which shall be satisfied before permission could be considered

(3) When applying for approval to manufacture a new drug under sub-rule (I) or its preparations, to the State Licensing Authority, an applicant shall produce along with his application, evidence that the drug for the manufacture of which application is made has already been approved by the Licensing Authority mentioned in Rule 21:

Provided that the requirement of submitting the results of local clinical trials may not be necessary if the drug is of such nature that the Licensing Authority may, in public interest, decide to grant such permission on the basis of data available from other countries:

Provided further that the submission of requirements relating to Animal Toxicology, Reproduction studies, Teratogenicity studies, Perinatal studies, Mutagenicity and Carcinogenicity may be modified or relaxed in case of new drugs approved and marketed for several years in other countries if he is satisfied that there is adequate published evidence regarding the safety of the drug, subject to the other provisions of these rules."

126. Rule 122B provides the procedure for obtaining the approval for manufacturing and/or sale of the new drug. Rule 122A pertains to the application for permission to import new drug. The language and requirements of both rules are almost similar except for purposes. The Rule 122B provides the procedure in two circumstances:

a) In the first circumstances, the party seeks permission for manufacturing of new drugs and its formulations;

b) In the second circumstances, the party seeks permission to import new drugs (bulk drug substance) and further seeks for the approval to manufacture using the bulk drug substance.

The procedure to be applied for first circumstance:

To get the approval for manufacturing the new drug (i.e. bulk drug) and its formulation, the applicant is required to make an application on Form 44 to the licensing authority. The term "Licensing Authority" is defined in Rule 21B, which reads as:

"Rule 21(B): "licensing authority" means the authority appointed by the Central Government to perform the duties of the licensing authority under these Rules and includes any person to whom the powers of a licensing authority may be delegated under Rule 22."

126.1 In India the licensing authority for new drugs is "Drug Control Authority of India". The typical fee that needs to accompany Form 44 is INR 50,000. While applying for the approval on Form 44, the applicant is required to submit data as given in Appendix I to Schedule Y. This Appendix I to Schedule Y is attached to this opinion.

126.2 The said exemptions from conducting local clinical trials and abbreviation of tests provided under Rule 122B(3) of the Drugs Rules are applicable only when the same drug sought to be manufactured in India by an applicant has already been approved and marketed in other countries for several years by the same applicant and based on data generated in global clinical trials by the same applicant. The exemption if any under Rule 122B(3) can only be available to the party who has already got the approval and marketed in other countries for the same drug. The plaintiffs are entitled to rely on their global trial data for approvals in India.

126.3 In addition to this data the applicant is required to include the results of clinical trials carried out in India in accordance with the guidelines specified in Schedule Y, along with the report of the clinical trials, which should be given in the format as shown in Appendix II.

126.4 On receiving the application accompanied by the (a) data; (b) results of clinical trials and (c) the clinical trial reports, the drug controller (Licensing Authority) must satisfy himself that the drug to be manufactured (bulk drug substance) or in the form of a finished formulation is effective, and safe for use in India. If the drug controller is satisfied, he will issue an approval on Form 46. If the drug controller is not satisfied, for instance, if the data provided or generated on the drug is not adequate, he must intimate the applicant in writing and also give conditions, which if fulfilled will satisfy him for the grant of the approval.

127. The procedure to be followed for second circumstance:

In second circumstance the drug is already approved outside India, but has not been approved in India and the applicant seeks to obtain the grant of approval to manufacture formulations, such an application also needs to be made on the same

Form 44 and the application procedure is the same as in first circumstance, excepting that the information and data is required to be submitted as per Appendix IA of Schedule Y.

In the case of second circumstance, no clinical trial or report is necessary but if the party wants to import a new drug, the applicant needs to perform:

1) Bioavailability/Bioequivalence and comparative Dissolution Studies, for oral dosage form.

2) Sub-acute animal toxicity studies for intravenous infusions and inject ables.

These studies need to be conducted with the pre-approval of the licensing authority. Other conditions of first circumstance apply. Once, the licensing authority is satisfied, he will issue the approval on Form 46A. There is also a further approval envisaged in Rule 122B and that is if the same party who has obtained an approval of a new drug wants an approval to market the drug either: (i) in modified dosage form or (ii) with new claims.

128. The defendant No. 3 in its application in Form 44 for manufacturing and marketing authorisation for the defendants' drug submitted data under "Permission to market a new drug" and not under "Subsequent approval / permission for manufacture of already approved new drug".

129. As the drug of the defendant No. 3 is biosimilar and is not identical drug to the innovator drug, it has to be called as new drug discovered by the defendant No. 3 who itself submitted that it has conducted various clinical trials independently.

130. As the defendants' drug is a new drug manufactured in India for the first time by defendant No. 3, paragraph 1(1)(iv)(a) of Schedule Y, which mandates that all phases of the clinical trials must be conducted in India, is applicable to the defendants' drug; accordingly, defendant No. 1 had no legal basis for exempting defendant No. 3 from conducting Phase I and Phase II of the clinical trials in the present case.

131. It is the admitted position that pursuant to the letter dated 23rd April, 2012, the Review Committee on Genetic Manipulation (the "RCGM") directed defendant No. 3 to approach defendant No. 1 for obtaining approval for conducting all phases of clinical trials (Phase I to Phase IV) in relation to the defendants' drug.

132. The defendant No. 3 by its letter dated 19th May, 2012 has given the following justification as to why the defendant No. 3 has not conducted the clinical trials of Phase I and Phase II:

"2. Justification as to why you are not carrying Phase I and II clinical trial

Trastuzumab is approved in India for more than a decade (12 years) and has shown good efficacy and safety in Indian population. To summarise our rationale for directly proceeding with a Phase III study are

The proposed Phase III study of R-TPR-016 will generate product-specific credible data with standard endpoints like overall response rate (ORR), progression free survival (PFS), and overall survival (OS).

The proposed study will also evaluate pharmacokinetics which is often an objective of a Phase I study.

The proposed study will also evaluate efficacy and safety which is an aim of a Phase II study."

133. If there had been no requirement under the Drugs Act and the Drugs Rules to conduct Phase I and Phase II clinical trials, defendant No. 1 would not have sought such an explanation from defendant No. 3. In any event, in the letter while explaining why defendant No. 3 was directly conducting Phase III clinical trials in relation to the defendants' drug, defendant No. 3 did not seek an exemption on the basis that the defendants' drug was a new drug already approved. The reasons for exemption mentioned in the aforesaid letter also do not find support in any provision of the Drugs Act or the Drugs Rules.

134. It appears from the record that without assigning any reason or speaking order even formal one at the asking or justification given by the defendant No. 3

the matter was proceeded with whereby the defendant No. 3 was asked to conduct the clinical trials on Phase III directly.

135. In Form 44 dated 21st March, 2015 at item No.2 A(5) it was stated by the defendant No. 3 before the Regulatory Authority that Exploratory Clinical Trials are not conducted of Phase II as the same was not applicable.

136. Similarly in at item No.2 (B), (C) and (D) the following statement was made in the annexures sent along with Form-44:

"B. Subsequent approval/permission for manufacture of already approved new drug: - (Not Applicable)

(a) Formulation:

(1) Bio-availability/Bio-equivalence protocol

(2) Name of the Investigator/canter

(3) Source of raw material (bulk drug substances) and stability study data.

(b) Raw material (bulk drug substances)

(1) Manufacturing method

(2) Quality control parameters and/or analytical specification, stability report.

(3) Animal toxicity data.

C. Approval/Permission for fixed dose combination:- (Not Applicable)

(1) Therapeutic Justification (Authentic literature in pre-reviewed journals/text books)

(2) Data on pharmacokinetics/pharmacodynamics combination

(3) Any other data generated by the applicant on the safety and efficacy of the combination.

D. Subsequent Approval or approval for new indication - new dosage form: (Not Applicable)

(1) Number and date of Approval/permission already granted.

(2) Therapeutic Justification for new claim/modified dosage form.

(3) Data generated on safety, efficacy and quality parameters."

137. Similarly in addition to explanation already given in the annexures by the defendant No. 3, the extract of the Enclosure 3 about the justification as to why the defendant No. 3 did not carry Phase I and Phase II of clinical trial including certain pre clinical studies, reads as under:

"Justification for not doing Trastuzumab Phase I and Phase II studies:

Introduction:

Trastuzumab is a humanized IgG1 kappa monoclonal antibody that selectively binds with high affinity to the extracellular domain of the human epidermal growth factor receptor 2 protein, HER21

Trastuzumab is approved for HER2 over expressing breast cancer and HER2-over expressing metastatic gastric or gastroesophageal junction adenocarcinoma.

In pivotal first line metastatic breast cancer (MBC) trials, the addition of Trastuzumab to standard systemic chemotherapy treatment resulted in significantly improved time to disease progression, improved response rates, and an overall survival benefit (as compared with chemotherapy alone). Consequently, single-agent Trastuzumab in combination with chemotherapy is now considered standard treatment for MBC patients who over express HER2. In clinical practise, Trastuzumab is usually continued until disease progression.

Trastuzumab has been approved in India, US, EU and ROW countries for more than a decade now. Trastuzumab was approved in India in July 2000. It was first approved in US in 1998.

R-TPR-016 (RLS Trastuzumab) development:

Manufacturing

Trastuzumab (R-TPR-016) developed by Reliance Life Sciences (RLS) is highly purified preparation that has been shown to be similar to innovators product Herceptin via multiple physic-chemical tests as well as shows comparable binding to HER2 expressing cells.

Trastuzumab has been produced by recombinant DNA technology using genetically engineered Chinese Hamster ovary cells (CHO) into which the Trastuzumab gene has been introduced. The drug substance (DS) contains Trastuzumab in a buffer that has the same components as in the final drug product of Herceptin.

Stability testing

Stability testing which is an integral part of product development has also been conducted for R-TPR- 016 in compliance with ICH guidelines for stability testing and as per published literature of innovator Trastuzumab. The results show that the product is stable at recommended as well as accelerated temperature.

Preclinical studies

RCGM, through the letter No. BT/BS/17/46/2001- PID dated November, 18, 2010 had approved the conduct of the following studies;

1. Single Dose Toxicity Study of Trastuzumab in Wistar Rats by Intravenous Route.

2. Single Dose Toxicity Study of Trastuzumab in Swiss albino mice by Intravenous Route.

3. 28-day Repeated Dose Toxicity Study of Trastuzumab in Wistar Rats by Intravenous Route.

4. 28-day Repeated Dose Toxicity Study of Trastuzumab in New Zealand White Rabbits by Intravenous Route.

5. Skin Sensitisation Study Trastuzumab in Guinea Pigs (Maximisation Test)

Results of the toxicology studies conducted for RTPR-016 reveal no toxic effects at the highest dose tested.

R-TPR-016 has undergone all mandatory preclinical studies with acceptable results in compliance with Indian regulatory requirements.

Clinical study

The proposed Phase III study is a prospective, multi-centric, open-label, two-arm, parallel group, active control, randomised comparative clinical study in metastatic breast cancer patients.

This study has endpoints like overall response rate (ORR), progression free survival (PFS), and overall survival (OS).

This study also has a pharmacokinetic comparison between R-TPR-016 and Herceptin.

Rationale of not doing a Phase I and II study :

R-TPR-016 has been manufactured in the same way as Herceptin.

R-TPR-016 also has an acceptable stability data as per regulatory guidances.

R-TPR-016 has undergone a battery of preclinical studies (approved by RCGM) and has shown good results in the same.

Trastuzumab is approved in India for more than a decade (12 years) and has shown good efficacy and safety in Indian population.

The proposed Phase III study of R-TPR-016 will generate product-specific credible data with standard endpoints like ORR, PFS and OS.

The proposed study will also evaluate pharmacokinetics which is often an objective of a Phase I study.

The proposed study will also evaluate efficacy and safety which is an aim of a Phase II study."

138. It is evident that as per Rule 122DA of the Drugs Rules mandates that all three phases of human clinical trials be conducted for a 'new drug' (as defined under Rule 122E of the Drugs Rules). Paragraph 2(7)(i) of Schedule Y of the Drugs Rules further provides that clinical trials should be conducted in a sequential manner, i.e., the data generated in Phase I clinical trials should form the basis of Phase II clinical trials and similarly, the data generated in Phase I and Phase II of the clinical trials should form the basis of Phase III clinical trials. Also, under paragraph l(l)(iv) of Schedule Y of the Drugs Rules, for new drug substances discovered in India, clinical trials are required to be carried out in India from Phase 1 onwards. Further, Clause 8 of the Biosimilar Guidelines mandates that all three phases of human clinical trials must be carried out for a biosimilar drug. Therefore a biosimilar drug is required to be subject to the full rigour of all phases of clinical trials, as envisaged under the Drugs Act read with the Drugs Rules and the Biosimilar Guidelines.

139. It appears from record that defendant No. 1 approved a clinical trial protocol submitted by defendant No. 3 in relation to TrastuRel (the "defendant's CTR") on 29th October, 2013. The said protocol was registered with the Clinical Trial Registry of India (the "CTRI") by defendant No. 3 on April 12, 2013 (registration No. CTRI/2013/04/003549). The defendant's CTR reflects that TrastuRel was allegedly tested for efficacy and pharmacokinetics end-points on 105 patients with solely HER 2+ metastatic breast cancer. It is apparent that the Clinical Trial Registry has examined the clinical trials of Phase III only.

140. Admittedly no clinical trials of Phase I and Phase II have been conducted by defendant No. 3 for TrastuRel which is not denied by the defendant No. 3, even otherwise if all the clinical trials were conducted and combined with Phase III, it was very convenient for the defendant No. 3 to get them also registered with the Authority. As per law Phase III studies are intended to confirm the evidence

accumulated in Phase II clinical trials effectiveness of the drug. Skipping phases of clinical trials is not justified under Rule 122DA and Paragraph 2(7)(i) of Schedule Y of the Drugs Rules, which mandate sequential clinical trials. Further Paragraph l(iv)(a) of Schedule Y of the Rules clearly states that for new drug substances discovered in India [TrastuRel], clinical trials are required to be carried out in India right from Phase I and data should be submitted as required under Items 1, 2, 3. 4, 5 (data, if any, from other countries) and 9 of Appendix I. There is no speaking order in writing that the defendant No. 1 has specially abbreviated the clinical trials of Phase I and Phase II.

141. In its application for manufacturing approval in Form 44 of the Drugs Rules to defendant No. 1 (the Form 44 Application), defendant No. 3 has not claimed that its application does not relate to subsequent approval for an already approved new drug i.e. rightly so. Accordingly, contrary to the submissions of defendant No. 3, no abbreviation of clinical trials was granted/allowed to TrastuRel.

142. In the meeting held on September 19, 2012, the New Drugs Advisory Committee (the "NDAC") had recommended defendant No. 3 to submit pharmacokinetic data relating to TrastuRel to the defendant No. 1 prior to conducting the "second part of the study", clearly indicating that the different phases of clinical trials were to be conducted separately. Such recommendation was further endorsed by the Technical Committee on March 27, 2014 as well as the Apex Committee on April 15, 2014. It is the admitted position that despite directions of the NDAC, Technical Committee and Apex Committee, defendant No. 3 conducted only Phase III clinical trials pursuant to its application to defendant No. 1 dated 16th February, 2012. Even, if any steps are taken by the defendant No. 3 or to combine with Phase III, however, the fact remains that trials of Phase I and Phase II or part thereof have not been registered with the defendant No. 1. Under paragraph 2(6) of Schedule Y of the Drugs Rules and item 5 of Appendix I and Clause 8.1 of the Biosimilar Guidelines, a Phase I clinical trial, which may be conducted in healthy volunteer subjects or certain types of patients, should include end points to test pharmacokinetics, pharmacodynamics, maximum tolerated dose and early measurement of drug activity. An important objective in Phase II clinical trials is to explore the dosage of the proposed drug. Since a biosimilar is never

identical to the reference biological product, in the absence of separate and independent Phase I and Phase II clinical trial for TrastuRel, it is unfair to assume that the Phase I and Phase II data for TrastuRel would be the same as the plaintiffs' Trastuzumab. It is not for the Court or for the regulatory authority to exempt the same suo motu or a party can allege that implied impliedly they have abbreviated in the absence of express provision of the Act because of the reason that it was the requirement of rules, the same cannot be ignored unless amendments are made in the Act and Rules, whereby in bio-similar drug the provision is made to exempt the clinical trial in particular nature of the case.

143. The said position is also fortified from the letter dated July 28, 2011, when the Review Committee for Genetic Manipulation (the "RCGM") directed defendant No. 3 to approach defendant No. 1 to obtain approval for conducting clinical trials for TrastuRel, and contrary to defendant No. 3's submissions, did not recommend the skipping of any phases of clinical trials. Accordingly, directly carrying out Phase III clinical trials by defendant No. 3 is completely unwarranted. The defendant No. 3 did not seek the RCGM approval was sought to waive Phases I and II of the clinical trials except the defendant No. 3 had informed that it was not required.

144. The contention of the plaintiffs is that with regard to clinical trials of Phase III of clinical trials, the end points in the defendant's CTR are contrary to the specifications under the Drugs Act read with the Drugs Rules and Biosimilar Guidelines. Under paragraph 2(8)(i) of Schedule Y of the Drugs Rules, Phase 111 clinical trials confirm the therapeutic benefits and the safety and efficacy of the drug. Further, under Clause 8.3 of the Biosimilar Guidelines, confirmatory safety, efficacy and immunogenicity clinical trials to demonstrate the similarity in safety and efficacy profiles of the purported biosimilar and the innovator biological drug are critical for the approval of a biological drug as a 'biosimilar'.

145. In its application in Form 44 of the Drugs Rules dated March 27, 2015 to defendant No. 1 filed by defendant No. 3 who sought manufacturing authorisation for TrastuRel for all the Indications despite having conducted clinical trials only on patients with HER2+ metastatic breast cancer. On the basis of such application, the Subject Expert Committee (Oncology and Haematology) (the "SEC")

recommended the grant of marketing authorisation to TrastuRel on May 7, 2015 (the "SEC Recommendation") TrastuRel for all the Indications despite the defendant's CTR reflecting that tests were conducted only on patients with HER2+ metastatic breast cancer.

146. The material placed by the defendant No. 3 which is accepted by the defendant No. 1 similar to Appendix I-A to Schedule Y of the Drugs Rules is not applicable to the approval of biosimilars for new drug. The application for approval of the drug included data in Appendix I which requires a complete set of trials to be conducted for a 'new drug' as bio-similar and not as per Appendix I-A. In the present case, it has been noticed that defendant No. 3 was processing its application in the manner to give its impression that it is no new drug within the meaning of Rule 122E being DNA (r-DNA) derived drug, on the other hand the defendant No. 1 is proceeding with the prescribed application under the Appendix IA and as per requirement of Appendix I without following the procedure.

147. The chart which contains the details of regulatory regime under the Drugs and Cosmetics Rules, 1945 (the "Drugs Rules") for approval of various categories of drugs, is as under:

Category of drug	Relevant part of the Drugs Rules	Applicable provision of the Drugs Rules for approval for import/manufacture	Relevant forms for application and approval	Relevant Schedule of the Drugs Rules, if any	Whether Appendix IA of Schedule Y is applicable

Biologic (r-DNA) drug	Part XA	Import - Rule 122A Manufacture-Rule 122B	Application for Import-Form 44 Approval for Import - Form 45/Form 45A Application for Manufacture-Form 44 Approval for Manufacture-Form 45/Form 46A	Schedule Y	Appendix I
Biosimilar (r-DNA) drug	Part X A	Import-Rule 122A Manufacture Rule 122B	Application for Import-Form 44 Approval for Import - Form 45/Form 45A Application for Manufacture-Form 44 Approval for Manufacture -Form 46/Form 46A	Schedule Y	Appendix I

Chemical innovator drug Chemical generic - innovator approved for less than 4 years + innovator not approved in India (but in otter countries)	Part XA	Import-Rule 122A Manufacture -Rule 122B	Application for Import-Form 44 Approval for Import - Form 45/Form 45A Application for Manufacture -Form 44 Approval for Manufacture -Form 46/Form 46A	Schedule Y	Appendix I
Chemical generic - innovator approved for less than 4 years + innovator approved in India	Part XA	Import - Rule 122A Manufacture Rule 122B	Application for Import - Form 44 Approval for Import - Form 45/Form 45A Application for Manufacture - Form 44 Approval for Manufacture -Form 46/Form 46A	Schedule Y	Appendix I

	Part XA	Import-Rule 122A Manufacture Rule 122B	Application for Import - Form 44 Approval for Import - Form 45/Form 45A Application for Manufacture -Form 44 Approval for Manufacture - Form 46/Form 46A	Schedule Y	Appendix IA
Chemical generic-innovator approved for more than 4 years	Part VII	Application to manufacture-Rule 69 LIcence to manufacture Rules 70 and 71	Application to manufacture Form 24 Licence to manufacture - Form 25	Schedule M	Not applicable

148. The specimen of requirement under Appendix I of the Drugs and Cosmetics Rules, 1945 by defendant No. 3 as well as the details of alleged clinical trials not conducted by the defendant No. 3 as per chart supplied by the counsel for the plaintiffs are reproduced as under:

Provision and requirement under Appendix I of he Drugs and Cosmetics Rule, 1945.

1.Introduction

A. Brief description of the drug and he therapeutic class to which it belongs.

2. Chemical and pharmaceutical information.

2.1. Information on active ingredient's Drug information (Generic Name, Chemical Name of INN)

2.2 Physicochemical Data

(a) Chemical name and Structure

Empirical formula

Molecular weight

(b) Physical properties

Description

Solubility

Description

Solubility

Rotation

Partition coefficient

Dissociation constant

2.3 Analytical Data

Rlemental analysis

Mass spectrum

NMR. spectra

IR spectra

UV spectra

Polymorphic identification

2.4. Complete monograph specification including

Identification

Identity/quantification of impurities

Enantiomeric purity

Assay

2.5 Validations

Assay method

Impurity estimation method

Residual solvent/other volatile impurities (OVI) estimation method

2.6 Stability Studies (for details refer Appendix (IX)

Final release specification

Reference standard characterisation

Material safety data sheet

2.7 Data on Formulation

Dosage form

Composition

Master manufacturing formula

Details of the formulation (including inactive ingredients)

In process quality control check

Finished product specification

Excipient compatibility study

Validation of the analytical method

Comparative evaluation with international brand(s) approved Indian brands, if applicable

Pack presentation

Dissolution

Assay Impurities

Content uniformity

PH.

Force degradation study

Stability evaluation in market intended pack at proposed storage conditions.

Packing specification

Process validation

When the application is for clinical trials, only, the international non-proprietary name (INN) or generic name, drug category, dosage form and data supporting stability in the intended container-closure system for the duration of the clinical trial (information covered in item nos. 2.1, 2.3, 2.6, 2.7) are required.

3. Aninial Pharmacology (for details refer Appendix : IV)

SUMMARY

3.2. Specific pharmacological actions

3.3. General pharmacological actions

3.4. Follow-up and Supplemental Safety Pharmacology Studies

3.5. Pharmacokinetics: absorption, distribution; metabolism; excretion

4. Animal Toxicology (for details refer Appendix III)

4.1. General Aspects

4.2. Systemic Toxicity Studies

4.3. Male Fertility Study

4.4. Female Re-production and Developmental Toxicity Studies

4.5. Local toxicity

4.6. Allergenicity/FIypersensitivity

4.7. Genotoxicity

4.8. Carcinogenicity

5. Human/Clinical pharmacology (Phase I)

SUMMARY

5.2. Specific Pharmacological effects

5.3. General Pharmacological effects

5.4. Pharmacokinetics, absorption, distribution, metabolism, excretion

5.5. Pharmacodynamics/ early measurement of drug activity

6. Therapeutic exploratory trials (Phase II)

SUMMARY

6.2. Study report(s) as given in Appendix II

7. Therapeutic confirmatory trials (Phase III)

SUMMARY

7.2. Individual study reports with listing of sites and Investigators.

8. Special studies

SUMMARY

8.2. Bio-availability / Bio-equivalence.

8.3. Other studies e.g. geriatrics, paediatrics, pregnant or nursing women

9. Regulatory status in other countries

9.1. Countries where the drug is

a. Marketed

b. Approved

c. Approved as IND

d. Withdrawn, if any, with reasons

9.2. Restrictions on use, if any, in countries where marketed approved

9.3. Free sale certificate or certificate of analysis, as appropriate.

10. Prescribing information

10.1. Proposed full prescribing information

11. Samples and Xesting Protocol/s

11.1. Samples of pure drug substance and finished product (an equivalent of 50 clinical doses, or more number of clinical doses if prescribed by the Licensing Authority), with testing protocols, full impurity profile and release specifications.

149. Data required to be submitted by an applicant for grant of permission to import and/or manufacture a new drug already approved in the country as per Appendix I-A is as under:

1. Introduction

A brief description of the drug and the therapeutic class

2. Chemical and pharmaceutical information

2.1 Chemical name, code name or number, if any; non-proprietary or generic name, if any, structure; physico-chemical properties

2.2 Dosage form and its composition

2.3 Test specifications

(a) active ingredients

(b) inactive ingredients

2.4 Tests for identification of the active ingredients and method of its assay

2.5 Outline of the method of manufacture of active ingredients

2.6 Stability data

3. Marketing information

3.1 Proposed package insert/promotional literature

3.2 Draft specimen of the label and carton

4. Special studies conducted with approval of Licensing Authority

4.1 Bioavailability/Bioequivalence and comparative dissolution studies for oral dosage forms

4.2 Sub-acute animal toxicity studies for intravenous infusions and inject ables."

150. The explanation given by the learned ASG about the treating of application as per Appendix I-A of Schedule Y would reveal that the defendant No. 1 was not clear regarding the legal regime applicable to approval of biosimilars in India as it is apparent that the defendant No. 3 filed its application under Appendix I and the DCGI sought justification from defendant No. 3 for directly carrying out Phase III clinical trials. The defendant No. 1 failed to understand that it is not a generic drug but bio-similar product wherein the defendant No. 3's product is new drug which has not been approved in its favour either in India or any part of the world and the said defendant No. 3 has not separately generated the data in order to compare the data of the innovator and being a new drug, head to head comparison of the drug of defendant No. 3 and innovator is essential as per Rules. Although learned Senior counsel appearing on behalf of the defendant No. 3 has mentioned that in its laboratory head to head comparison has been conducted but at the same time, the defendant No. 3 is not prepared to give the inspection of the requisite documents asked by the plaintiffs during the course of hearing in the present case and in earlier suit, being CS(OS) No. 355/2014. If defendant No. 3's application was being considered under Appendix l-A as argued by defendant No. 1, the regulator would not have required such justification.

151. Paragraph 2(8)(iii) of Schedule Y of the Drugs Rules relates to a drug approved outside India, which admittedly the impugned drug is not. When defendant No. 3 had applied to defendant No. 1 for permission to directly conduct Phase III clinical trial, defendant No. 1 wrote to defendant No. 3 seeking an explanation from defendant No. 3 regarding the omission of Phase I and Phase II clinical trials. If there had been no requirement under the Drugs Act and the Drugs Rules to conduct Phase I and Phase II clinical trials for drugs, defendant No. 1 would not have sought such an explanation from defendant No. 3. Any reference to Paragraph 2(8)(iii) of Schedule Y of the Drugs Rules does not help the case of the defendant No. 3 as it is the plaintiffs' drug which was approved outside India. The exemption if any can only be granted to the plaintiffs under Rule 122A and 122B. The unexplained exemptions in the data requirements granted to defendant No. 3 during the process of approval of the drug are contrary to the Schedule Y. The said exemptions are permissible also in case of generic drug of bio-equivalent but not biosimilar if the drug in question is a new drug and if a party applies first

time for its approvals for manufacturing and marketing within the meaning of Rule 122 read with Schedule Y.

Paragraph 1(1)(iv)(b) of Schedule Y of the Drugs Rules relates to new drug substances discovered in countries other than India and any abbreviation of clinical trials contemplated in this provision is therefore not applicable to drug which was admittedly developed in India, even though it is applicable to the plaintiffs' Trastuzumab discovered outside India.

152. The claim of defendant No. 3's that the impugned drug not being a "new drug discovered in India" is not correct as the drug is admittedly an indigenously-developed drug. Rule 122DA read with paragraphs 1(1)(iv)(a), 1(1)(iv)(c) and 2(6) to 2(8) of Schedule Y of the Drugs Rules require that all three phases, i.e. phases I, II and III of human clinical trials be conducted for a 'new drug' in a sequential manner, i.e., the data generated in phase I clinical trials should form the basis of phase II clinical trials and the data generated in phase I and phase II of the clinical trials should form the basis of phase III clinical trials.

153. Defendant No. 1 has incorrectly stated that Appendix IA of Schedule Y of the Drugs Rules is applicable in relation to the defendants' drug. Appendix IA relates to data required to be submitted by an applicant for grant of permission to import and/or manufacture a new drug already approved in the country and the defendants' drug is not a new drug already approved in the country on the date of filing of application. I do not agree with the argument of defendants and I am of the view that the data required to be submitted for the approval of the defendants' drug is set out in Appendix 1 of Schedule Y of the Drugs Rules. In fact, defendant No. 3's application for permission to conduct clinical trials and for grant of manufacturing and marketing authorisation purportedly included information in Appendix I. Any reference under these circumstances to Appendix I-A in the Written Statement is evidently an afterthought and defendant No. 1 is merely seeking to justify the unexplained exemptions in the data requirements granted to defendant No. 3 during the process of approval of the defendants' drug.

154. Defendant No. 1's assertions that (a) Phase I and Phase II clinical trials are not mandatory under Schedule Y of the Drugs Rules for drugs already approved in

India or outside India; and (b) Schedule Y prescribes that for new drugs approved outside India, Phase III studies need to be carried out primarily to generate evidence of efficacy and safety of the drug in Indian patients, are not relevant in the present case since the defendants' drug was neither previously approved in India nor outside India.

155. The applications filed by defendant No. 3 for approval of TrastuRel contradict the contents of the Written Statement. Form 44 filed along with defendant No. 3's application for manufacturing and marketing authorisation was filed specifically under Rule 122B of the Drugs Rules, which relates to approval for manufacture of new drugs. Moreover, the manufacturing and marketing approval for the defendants' drug was granted by defendant No. 1 in Forms 46 and 46A under Rule 122B of the Drugs Rules. The entire Rule 122B along with provisos is to be read together with Rules and requirements of Schedule Y. The proviso of Rule 122B cannot be read in isolation. The defendant No. 3 itself had made the application in the prescribed form of Rule 122DA in Form-44. The clinical trials and studies and other documents are to be submitted as per Appendix I of Schedule Y whereby clinical trials of all phases are necessary and not as per Appendix I-A as there is vast difference in submitting the data between the two i.e. Appendix I and Appendix I-A. The said mandatory requirement was not noticed by the defendant No. 1 at the time of recommendation and approvals. Actually the same have been ignored.

156. In reply to this, it canvassed by the defendant No. 3 that the defendant No. 3 was entitled to follow an abbreviated process for approval since its application related to subsequent approval for an already approved new drug by the innovator of the drug.

157. It is submitted by defendant No. 3 that there is the system of abbreviated pathways in certain jurisdictions particularly on the European model i.e. Argentina, Australia, Brazil, Canada, Japan, Malaysia, Mexico, South Africa, South Korea, Taiwan and Turkey which allows regulatory authorities the discretion to consider whether certain phases of clinical trial are necessary for the application process for the follow-on biological drug or, alternatively, may be waived if similarity has

sufficiently been established at the stage of pre-clinical studies.

158. It is correct that the said practise is being followed in many countries. It is permissible subject to the condition if the regulatory authorities are satisfied that such waiver is (a) permissible in accordance with the rigorous standards of interchangeability and similarity with the innovator drug under applicable laws; (ii) scientifically justified pursuant to complete characterisation and preclinical studies having been concluded to establish comparability of the follow-on biologic drug with the innovator drug in terms of quality, safety and efficacy. Only after the fulfilment of these conditions by the follow-on drug manufacturer that the extent of possible reduction of pre-clinical and clinical trial data is determined by the regulatory authority, strictly on a case-by-case basis but never automatically.

159. In the present case, the defendant No. 1 pressing impliedly abbreviated many clinical tests but without any reason as appeared from the record submitted. The defendant No. 1 during the process of the application for approval, all the time whatever explanations are given by the defendant No. 3, the same are taken on record and proceeded further in the matter.

160. As per Paragraphs 5, 6(a), 7 and 8 of the WHO Guidelines on Evaluation of Similar Biotherapeutic Products, 2009 (the "WHO Guidelines") relied on by defendant No. 3, the entire set of characterisation and comparability studies under applicable law are to be carried out in a step-wise manner to establish similarity of the follow-on drug to the innovator drug in terms of quality. The conduct of such studies is a prerequisite for possible reduction of non-clinical and clinical data, if permitted by the drug authority. In the present case, admittedly the defendant No. 3 has not conducted studies in step-wise manner.

161. As mentioned above, it is the specific case of the plaintiffs that defendant No. 3 has not conducted (a) comparative product characterisation studies; (b) comparative animal pharmacology studies; (c) comparative immune response studies; or (d) comparative animal toxicology studies. Even if in many countries an abbreviated pathway is allowed for biosimilar drugs and existed in India but the drug authorities cannot permit the waiver of phases I and II of human clinical trials for the drug on account of the inadequate characterisation studies and pre-clinical

tests undertaken by defendant No. 3 for its drug. The party who is intentionally and deliberately even not ready to given the inspection of documents of clinical trials by making so many excuses by claiming confidentiality by filing of application. The plaintiffs got opportunity to address their submissions on this aspect. The counsel for the defendant No. 3 has tried to convince the Court by given two examples of third parties for the same drug by stating that they were exempted by the Regulatory Authority for Phase I and Phase II trials as evidenced in the international regime and contrary to the submissions of defendant No. 3, Celltrion has separately conducted Phase I and Phase II clinical trials in South Korea and the EU and Pfizer has separately conducted Phase I and Phase II clinical trials in the U.S.A. Thus, the submissions of the defendant No. 3 on this aspect are also wrong and misleading.

162. Let me now also evaluate the contention of the defendant No. 3 which relates to exemption to the clinical data requirement for the drugs relating to life threatening diseases. Sub-Rule 3 of Rule 1 of the Schedule Y 'Requirements and Guidelines for Permission to Import and/ or Manufacture of New Drugs for Sale or to undertake Clinical Trials' provides as follows:

"Paragraph 1(3) of Schedule Y -

For drugs indicated in life threatening / serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority."

The above rule of the Drugs Rules indicates that only in life threatening diseases, toxicology and clinical data requirements can be abbreviated, deferred or omitted, as deemed appropriate by the Approving Authority.

163. The defendant No. 3 submits that it is for the defendant No. 1 to decide as to whether all phases of clinical trials are required to be conducted in a particular case. Once a new drug is approved in other countries, there is no requirement to conduct all phases of clinical trials for a biosimilar drug (especially Phase I and II which are carried out on healthy volunteers). It is argued that in India, Professor

Ranjit Roy Choudhary Committee has recommended that in case of drugs already in the market and well regulated, only Phase IV clinical trials should be conducted.

It is argued by the defendant No. 3 that abbreviated pathway for approval of drug needs to be followed for approval of a follow on / biosimilar drug in view of various Guidelines and also the Drugs and Cosmetics Rules, 1945 which vest in the authorities, the discretion to abbreviate the pathway for approval of drugs (Refer Rule 122B read with Schedule Y: 1 (1) (iv) (b) and (c), Rule 1 (3)). Hence, there is no requirement to conduct the clinical trials for approval of a follow on drug.

164. As per the case of defendants that it has carried out Phase III study directly that was required for pharmacokinetic and pharmacodynamic studies as a part of phase III studies after getting mandatory approvals from competent authority. The phase III studies were also registered with the Clinical Trial Registry-India ('CTRI'). In fact, the 2012 Guidelines also contemplate that PD study can also be a part of Phase III clinical trials. The objective of a Phase I trial is to establish comparative pharmacokinetics (pK) and this pK data was generated by defendant No. 3 as the initial part of the Phase III trial. Defendant No. 3 did the Phase I and Phase II trials as part of the same sequential study, since it was necessary to do the pK study in patients and not in healthy volunteers. The defendant No. 3 admitted that it has not conducted Phase II study as dose finding and POC studies are not required for follow-on products (biosimilars or generics).

165. Paragraph 1(3) of Schedule Y of the Drugs Rules is only available for serious emergency situations such as an epidemic of an unknown disease and will not be applicable to a drug targeting a disease for which treatments are already available in the market (refer to paragraph 7.20 of the Parliamentary Committee Report on the Functioning of the CDSCO).

166. The defendant No. 3's reliance on paragraphs 1(1)(iv)(b), 1(3) and 2(8)(iii) of Schedule Y of the Drugs Rules would not help the case of defendant No. 3. Even there is nothing on record to indicate that exemptions under these provisions were sought by, or granted to, defendant No. 3 while conducting clinical trials for the drug. The reference to such exemptions is just an afterthought defence raised by the defendant No. 3 who is trying to insist that it should be implied by the Court.

There is no specific order of exemptions passed for Phase I and Phase II trials. The defendant No. 1 has merely proceeded further with process of approval after the explanation given by the defendant No. 3 for not conducting all the clinical trials of Phase I and Phase 2 in registration thereof with defendant No. 1.

167. Even as per paragraph 8 of the Guidelines on Similar Biologics, 2012 (the "Biosimilar Guidelines") mandates that all phases of comparative human clinical trials including pharmacokinetic, pharmacodynamics, confirmatory safety, efficacy and immunogenicity studies must be carried out for a biosimilar drug. Defendant No. 3 has tried to justify the deficiencies in the tests conducted for drug on the basis of paragraph 6 of the Biosimilar Guidelines which states that the extent of testing of the similar biologic is "likely to be less" than that required for the reference biologic. The said provision envisages possible reduction in pre-clinical and clinical data with the condition that the testing of the similar biologic must be "sufficient to ensure that the product meets acceptable levels of safety, efficacy and quality". Accordingly, such reduction may be permitted only if comparability with the innovator drug has been demonstrated at the characterisation stage and the production process of the similar biologic is consistent. The extensive pre-clinical and clinical evaluation is necessary for the similar biologic if significant differences in safety, efficacy and quality studies emerge.

168. The relaxation under this provision is only possible if a party would establish similarity between drug of defendant No. 3 and the plaintiffs' Trastuzumab, on account of incomplete product characterisation and pre-clinical studies having been conducted for the drug.

The defendant No. 3 in the present case even not ready to give the inspection of the documents which are used at characterisation stage, pre-clinical and clinical evaluation in order to allow the plaintiffs to make their submissions on merit but at the same time, the defendant No. 3 wishes to rely upon the entire data of the plaintiffs drug for the purpose of approval as well as at the time of marketing their product.

169. The explanation given by the defendant No. 3 by placing the reliance of para l(l)(iv)(b) of Schedule Y is not possible as the defendants' drug is a new drug

discovered in India. Para 1(1) (iv)(a) of Schedule Y is applicable which mandates that all phases of the clinical trials be conducted in India. Further, the defendant No. 3 did not have earlier approval in India or any part of the world. No such valid justification was given by defendant No. 3 in its letter to the DCGI which is acceptable under the Act, Rules as well as the Guidelines of Biosimilar, 2012.

170. The defendant No. 1 has incorrectly relied on Rule 122A i.e. Application for permission to import new drugs and Rule 122D (Permission to import or manufacture fixed dose combination), while the only applicable provision is Rule 122B (Application for approval to manufacture new drug) wherein the defendant No. 3 itself has filed the application in Form-44, Appendix I. Under the heading "subsequent approval/permission for manufacture of already approved new drug", in the form filed in the prescribed manner, it was mentioned "not applicable". The defendant No. 1 has treated the application of defendant No. 3 in Form 44-Appendix I as Appendix I-A in which clinical trials of all phases are not necessary. Even no written order was passed assigning any reason for abbreviation of Phase I and II and treating the application for the purpose of requirement of documents, clinical trials and studies under Appendix I-A or Appendix II. Merely saying that part of clinical which are conducted have been combined with the Phase III neither here nor there, it would be contrary to the scheme of the Act because these are to be registered with the Regulatory Authority under the provision of Act and Rules.

171. It cannot be said that the said enquiry and procedure of the grant of the approval shall be as simplistic as contended by the defendants wherein the defendant No. 3 makes an application for the conducting the clinical trial for phase III on presumptuous basis that the defendant No. 1 will allow the same with bare minimum justification of the underlying purpose of the other two phases of the trials and giving a response that the clinical trials are conducted in a combined manner when there is no evidence of the registration of the separate trials. Surely, the process of the similar biologic require as a matter of rule to conduct the clinical trials with exceptions apart to reduce the requirement of the data submission depending upon the establishment of the similarity on the various aspects, product characterisation, quality comparability studies and other matters discussed above.

172. It cannot be said on mere saying of the defendants that sufficient safeguards have been followed in granting the approval to the defendant No. 3 in relation to the bio similar medicines. After all, it is a matter of the safety, efficacy and quality of the medicine which is meant for treatment of cancer and involve complex compound requiring differential treatment prescribed by the defendant No. 1 itself and relevant department of the government.

173. The reliance of defendant No. 3 is that the clinical trials of Phase I and Phase II have been combined by the defendant No. 3 with the Phase III while seeking an approval from the defendant No. 1 in its reply addressed to the defendant No. 1 in response to letter when the defendant No. 1 asked for the justification for not conducting the clinical trial. A mere reply for non conducting of the Phase I and Phase II trials provides an evasive answer to state that both the trials have been combined with the phase III trial as end points. The defendant No. 1 thereafter did not pass any speaking order ruling on the reasoning accorded by the defendant No. 3 who implicitly allowed the defendant No. 3 to conduct Phase III trials directly and produce the same for the analysis. There is no provision in India or internationally in relation to an 'abbreviated pathway' in the form stated by defendant No. 3 for the approval of biosimilar drugs.

174. Prima facie it appears to the Court that the combining/ skipping various phases of clinical trials is not justified if all the requisite clinical trials are not conducted as it would render redundant the underlying logic of sequential testing vis-a-vis primary end-points, target population and sample size. Paragraph 7.3 of the Biosimilar Guidelines clearly provides that the RCGM recommends the required phases of clinical trials based on an assessment of the pre-clinical test results, paragraph 10 of the Office Order issued by the Department of Biotechnology bearing No. BT/BS/17/175/2005-PID and dated January 2, 2006 wherein the RCGM recommended that all four phases of clinical trials should be undertaken.

175. In the present case all responses coming from Drug controller are contrary from the guidelines on similar biologics headed over by drug controller himself stating that the regime of the bio similar products are required to be regulated

more strictly than the ordinary drug approvals in the case of bio equivalence and therefore strict rules and norms are required to be followed for the approval of bio similar products. It goes on to show that prima facie the response of the defendant No. 1 if it is to be taken on the basis of the submissions advanced by the defendant No. 1 in terms of regime relating to bio equivalence before this court. This is due to the reason that by presuming that the drug is already marketed in India and defendant No. 3 does not intend to bring new drug within the meaning of Rules of bio-similar, the defendant No. 1 has adopted the approach as it is processing the application for obtaining the approval in the regime of bio equivalence is simplified wherein the applicant has to only show that the medicine is bioequivalent to the medicine already marketed and on that basis, the clinical trials requirements can be relaxed.

176. In the present matter, the defendant No. 1 as a Drug Controller was dealing with new drug of defendant No. 3 (which cannot be identical in all respects as admitted by the defendants) who was seeking approval on the basis of claim of similarity of biological structure, composition and other characteristics and on the date of the granting the approval was already the participant in the guidelines requiring the stricter approach to be adopted in the case of the Bio Similar drugs. Thus, the question was not really before the defendant No. 1 that the drug was already marketed in India as stated by the defendant No. 1 in its written statement which normally eases the process of approval in the case of normal drugs, this has been admitted by the drug controller being party to the guidelines starting point of the guidelines commences from the departure to the approach of bio-equivalence. If that is the level of contradiction in the stand of the defendant No. 1 in the written statement, submissions advanced before this court vis-a-vis the guidelines framed on the similar biologics, then prima facie on the face of it, the approval granted by the defendant No. 1 appears to be on the basis of the regime of the bio-equivalence on the premise that the drug is already marketed in India would lead all others to derive the benefit of the seeking the approval on the said basis when the scheme of bio similar is a complete departure thus rendering the approval contrary to its own guidelines.

177. With regard to Choudhary Committee Report (2013) relied upon by defendant No. 3 is not applicable to the present dispute since the defendants' drugs were not on the market in well-regulated countries before being introduced in India in the year 2011. Rather said report goes against the defendants. The report recommends that Phases I to IV clinical trials of all new entities developed in India to be marketed in India will need to be carried out in India as per paragraph 16 on page 4 of the Report which also contemplates that only applications concerning national emergencies or drugs/biologicals for tropical diseases will receive priority for expedited review.

Two Additional Indications

178. It is a matter of fact that the original application for grant of the approval was filed for metastic breast cancer however, later on the approval of two additional indications under the license given i.e. for metastic early breast cancer and metastic gastric cancer.

179. It is the case of the plaintiffs that the defendant No. 3 was required to conduct detailed pre-clinical and clinical trials for the approval of TrastuRel for two additional indications under Rule 122E(b) of the Drugs Rules, a drug already approved by defendant No. 1 which IS proposed to be marketed for anew indication, is a "new drug" for the purposes of the Drugs Rules. It is necessary that the approval of such a "new drug" requires complete pre-clinical and clinical trials to be conducted by the applicant drug manufacturer. Defendant No. 3 has admittedly not undertaken any clinical trials for the Additional Indications, in complete violation of the Drugs Rules and Biosimilar Guidelines.

180. It is alleged that in view of terms of Clause D of Form 44 of the Drugs Rules, which form is required to be filed, inter alia, along with applications for approval for manufacture of new drugs, the applicant should provide therapeutic justification for the new claim and the data generated on safety or quality parameters. The Form 44 Application states that such application does not relate to subsequent approval for new indications and, accordingly, admittedly, no such therapeutic justification or data has been provided by defendant No. 3.

181. It is alleged by defendant No. 3 that the additional indications as sought to be approved by the defendant No. 3 are not beyond the already approved indications for which the plaintiffs' drug/reference drug has already been approved. The said practise is also internationally accepted. The extrapolation of indications is thus simply a case of administrative confirmation by the defendant No. 1 whereby the defendant No. 3 is permitted to manufacture and sell its biosimilar Trastuzumab for EBC and MGC indication.

182. The defendant No. 3 has not conducted any studies or tests in relation to two additional indications. The defendant No. 3 has sought to extrapolate the data generated and relied on first indication i.e. metastic breast cancer for additional indications. No data of safety and efficacy has been provided separately to the defendant No. 1 as admitted by the defendant No. 3.

183. The defendant No. 3 has tried to give justification for extrapolation of safety and efficacy data from one indication of trastuzumab to the additional indications. It is submitted that as per the Biosimilars Guidelines 2012, Clause 8.5, 'Extrapolation of Efficacy and Safety Data to Other Indications' Extrapolation of Efficacy and Safety Data of a Particular Clinical Indication (for which clinical studies has been done) for a similar biologic to other clinical indications may be possible if following conditions are met:

1. Similarity with respect to quality has been proven to reference biologic;

2. Similarity with respect to pre-clinical assessment has been proven to reference biologic;

3. Clinical safety and efficacy is proven in one indication;

4. Mechanism of action is same for other clinical indications;

5. Involved receptor(s) are same for other clinical indications;

184. It is submitted by the defendant No. 3 that in all approved clinical indication the involved receptor are the same and Trastuzumab shows its efficacy in approved clinical indication by interacting with HER2 protein and causing cell a

proptosis and interfering with downstream signals. As all these conditions were met for the additional indications, therefore the request for approval was made to the DCGI and on merit, the approval was accorded for all the 3 indications.

185. As per Rule 122E(b) of the Drugs Rules, a drug already approved by the DCGI which is proposed to be marketed for a new indication, is a "new drug" for the purposes of the Drugs Rules. There is no provision under the Drugs Act and the Drugs Rules permitting exemption from conducting such tests for approval of a biosimilar drug for new indications. As per Clause D of Form 44 of the Drugs Rules, which form is required to be filed, inter alia, along with applications for approval for manufacture of new drugs, the applicant should provide therapeutic justification for the new claim and the data generated on safety or quality parameters.

186. It is submitted by the plaintiffs that the extrapolation of the clinical data relating to one therapeutic indication to another different indication is not automatic or unqualified and must be therapeutically justified with safety and quality data. Such extrapolation is not justified in the case of TrastuRel for the Additional Indications because the endpoints for a clinical trial for metastatic stage cancer are different from the end-points for an early stage cancer, including in relation to the safety and efficacy. In particular, it is an accepted medical fact that metastatic breast cancer cannot be cured, it can only be treated to prolong the patents life; therefore, the drugs targeting metastatic breast cancer aim to control the growth of the cancer and/or to relieve symptoms caused by it. Conversely, early breast cancer can be cured in some cases. Accordingly, the appropriate clinical trial end points for a drug targeting HER2+ early breast cancer is disease free survival, which measures the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer. Disease free survival cannot be the end point for HER2+ metastatic breast cancer.

187. It is evident that the extrapolation of the clinical data relating to one therapeutic indication to another different indication is not automatic or unqualified and must be therapeutically justified with safety and quality data.

It cannot be disputed that the appropriate clinical trial end points for a drug targeting HER2+ early breast cancer is disease free survival, which measures the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer.

188. For clinical trials in relation to HER 2+ metastatic breast cancer, the patient population is heterogeneous, which adversely affects the clinical outcome. On the contrary, clinical trials for HER2+ early breast cancer would be conducted on a homogeneous patient population, which would be a sensitive clinical trial test model to show the potential differences with the innovator biological drug.

189. There is no material on record to show that TrastuRel has been and the defendant No. 1 was certain that if it could also cure the other two additional indications as the defendant's CTR is restricted to patients suffering from the incurable HER2+ metastatic breast cancer. Accordingly, the results of clinical trials purportedly conducted on TrastuRel in relation to HER2+ metastatic breast cancer cannot be relied upon by defendant No. 3 for approval of the TrastuRel for the Additional Indications. International practices do not permit immunogenicity data in immunosuppressed subjects to be extrapolated to an indication in healthy subjects or patients with autoimmune diseases, and therefore, data from HER 2+ metastatic breast cancer relating to tests conducted with immunosuppressed subjects cannot be extrapolated to HER2+ early breast cancer.

190. It is informed by the learned Senior counsel for the plaintiffs that the approval of the plaintiffs' Trastuzumab, which is the innovator drug in the present case, for HER2+ early breast cancer and HER2+ metastatic gastric cancer in India took almost 4 years and years respectively from the initial approval for HER2+ metastatic breast cancer and was based on global clinical trials conducted by the plaintiffs.

191. It is submitted by the plaintiffs that the defendant No. 3 has not conducted any clinical trial test model which could detect potential differences between the drug of the defendant No. 3 and the plaintiff's Trastuzumab. HER 2+ metastatic breast cancer is not a sensitive clinical trial test model to detect potential differences in safety, efficacy and immunogenicity. The pharmacokinetics would

be affected because of the patient's health status and tumor burden and the international practices do not permit immunogenicity data in immunosuppressed subjects to be extrapolated to an indication in healthy subjects or patients with autoimmune diseases, and therefore, data from HER 2+ metastatic breast cancer relating to tests conducted with immunosuppressed subjects cannot be extrapolated to HER2+ early breast cancer.

192. It is also submitted that the clinical trials for HER2+ early breast cancer would be conducted on a homogeneous patient population, which would be a sensitive clinical trial test model to show the potential differences with the innovator biological drug and the identification of data from a treatment-free follow-up phase which is crucial for the comprehensive characterisation of the immune response.

193. It is also submitted by the plaintiffs that the findings of the SEC Recommendation are not based on the clinical trials purportedly conducted by defendant No. 3 in relation to TrastuRel since the defendant's CTR clearly stated that studies were purportedly only conducted on patients with HER2+ metastatic breast cancer, while the SEC has inexplicably recommended TrastuRel for the Additional Indications, as well. Accordingly, defendant No. 1 should be enjoined from acting in furtherance of the SEC Recommendation and from granting marketing authorisation to TrastuRel. The SEC has made no observation in relation to the safety and efficacy of TrastuRel.

194. It is stated that in order to be considered biosimilar to the plaintiffs' Trastuzumab, TrastuRel is required to be tested for all the Indications that the plaintiffs' Trastuzumab is capable of treating, i.e. HER 2+ metastatic breast cancer, HER 2+ metastatic gastric cancer and HER 2+ early breast cancer. As stated above, the defendant's CTR reflects that the TrastuRel is not tested for the Additional Indications, i.e. HER 2+ metastatic gastric cancer and HER 2+ early breast cancer. TrastuRel cannot be considered to be biosimilar to the plaintiffs' Trastuzumab in the absence of the requisite trials for all the Indications.

195. Defendant No. 3 sought approval from defendant No. 1 for the carton, label and package insert for TrastuRel pursuant to its letter dated October 20, 2015. Subsequently, the package insert for TrastuRel was recommended for approval

with certain modifications and conditions by the SEC on October 27, 2015 (the "Package Insert Recommendation"). Defendant No. 3 has now obtained the final approval of defendant No. 1 for the package insert for TrastuRel after amendment of package insert and during the pendency of the suit as per record submitted by the defendant No. 1.

196. TrastuRel, as claimed by defendant No. 3, has been developed for the treatment of all the Indications, no clinical trials were conducted for two additional indications in relation to Trastuzumab. The defendant No. 3 has also relied upon the CTR which would show that defendant No 3 has purportedly conducted clinical trials to compare TrastuRel with HERCEPTIN. and it is stated that on the basis of the SEC Recommendation for the Manufacturing Authorisation was the alleged comparability of TrastuRel with the plaintiffs' Trastuzumab, therefore, the Manufacturing Authorisation for TrastuRel from defendant No. 1 is with respect to biosimilar version of the plaintiffs' Trastuzumab/ HERCEPTIN. and approvals are rightly granted.

197. In the foregoing paragraphs as discussed, it appears that TrastuRel has not been adequately tested to be termed as a biosimilar product. It is incorrectly claimed by defendant No. 3 as a biosimilar or comparable version of the plaintiffs' Trastuzumab/ HERCEPTIN. Linking of TrastuRel with the plaintiffs' Trastuzumab/ HERCEPTIN. would likely to harm the market of the plaintiffs' Trastuzumab/ HERCEPTIN. It may lead to a dilution of the plaintiffs' reputation and goodwill.

198. Prima facie, as stated above in the preceding paras, (a) the approval of the defendant's CTR two additional indications by defendant No. 1 on October 29, 2012; (b) the clinical trials purportedly conducted by defendant No. 3 pursuant to the defendant's CTR; (c) the SEC Recommendation relating to the grant of a marketing authorisation to TrastuRel for all the Indications; (d) the subsequent grant of the Manufacturing Authorisation by defendant No. 1; and (e) the launch of TrastuRel in the absence of the above referenced marketing authorisation and package insert approvals are not strictly as per the provisions of the Drugs Act, the Drugs Rules and the Biosimilar Guidelines.

199. Thus, it is yet to be established by the defendant's CTR about compliance with the Drugs Act, the Drugs Rules and the Biosimilar Guidelines who is bound to establish comparability or biosimilarity between TrastuRel and the plaintiffs' Trastuzumab on the basis of tests purportedly conducted pursuant to the defendant's CTR and TrastuRel is not biosimilar to the plaintiffs' Trastuzumab. The plaintiffs are entitled to inspect the documents on this aspect and would be entitled to raise their pleas. It can only happen after inspection of requisite documents.

200. It shows prima facie that the recommendation is not based on the clinical trials purportedly conducted by defendant No. 3 in relation to two additional indications. The studies and trials whatever conducted by the defendant No. 3 on patients are only in relation to with HER2+ metastatic breast cancer for which the original application was filed for clinical test was made for metastic breast cancer. Approval of two additional indications was granted by without passing the speaking orders and discussion.

201. When the approval of first indication itself is not granted strictly as per rules and guidelines.

202. The approval of two additional indications was granted admittedly without any clinical trials. Thus, the benefit of approval of extrapolation of clinical trial relating to one therapeutic indication to different. The same is supposed to be examined in a very careful manner in view of the drug involved in the matter.

203. The approval of such nature cannot be granted in mechanical manner or on demand. The authority has to assign reasons. The Regulatory Authority has to justify the claim of the applicant in writing while keeping in mind that the party is getting the benefit of such approval of extrapolation. Thus, the process of the approval of first indication should be more stringent and strict as per law and guidelines in view of the main reason that an extrapolation is not based on clinical trials.

TRASTUZUMAB

204. Similar arguments are addressed by both parties as in CS (OS) 355/2014, the earlier suit. The documents referred to are also same. Thus the finding would remain the same. It is a matter of fact that the defendant No. 3 has been granted the approval of the name Trastuzumab which is one of the International Non-proprietary Names (INN) who is proposed to use the said name in its carton(s) and package insert and data for the purposes of promoting their products. The materials would be shown to doctors, hospitals and patients in order to claim biosimilar drug by the defendant No. 3.

205. It is the case of the defendant No. 3 that as per the 'World Health Organisation Guidelines on the use of International Non-proprietary Names (INNs) for Pharmaceutical Substances', an INN identifies a pharmaceutical substance by a unique name that is globally recognised and is a public property.

206. It is argued that the aim of the INN system has been to provide health professionals with a unique and universally available designated name to identify each pharmaceutical substance unlike the brand name of a particular company, the INN name is the name of the bulk medicine itself and has to be printed on every product containing the said drug as the generic and biosimilars of known substances are identified with the same INN name. In the present case, the plaintiffs cannot claim monopoly or ownership over the same as it is a public property. It is submitted that as the defendant No. 3 has obtained all approvals for manufacturing and marketing Trastuzumab (marketed as TrastuRel) and therefore it is essential for the defendant No. 3 to refer to the INN name Trastuzumab for the convenience of the doctors and patients across the globe.

207. The case of the plaintiffs is that the INN "Trastuzumab" has been assigned by the WHO to the plaintiffs' innovator biologic drug. "Trastuzumab" is a biologic drug which is a recombinant DNA-derived humanised monoclonal antibody. INN Trastuzumab cannot be used by any party unless comparative tests establishing biosimilarity have been conducted.

208. Extracts from the WHO policy which are referred by learned senior counsel on behalf of the defendant No. 3 are set out below:

"The INN Programme's purpose is to assign non-proprietary names to medicinal substances so that each would be recognised globally by a unique name. INNs facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognised and is public property. In fact, unlike trade names, INNs do not give proprietary rights and can be freely used since they are in the public domain. The INNs form an essential part of the regulatory process in many countries where a non-proprietary name is required for licensing"

(emphasis supplied)

209. It is argued on behalf of defendants that the plaintiffs may have goodwill in the brand name HERCEPTIN and not in "Trastuzumab". "Trastuzumab" is an INN, it represents a drug of the plaintiffs for the last many years which has an intrinsic goodwill attached to such drug. The patent right in the drug in question has expired in 2013. Originally the said name may have been exclusively associated with the innovator drug but it cannot be called as brand name. It is a non-proprietary name. The new concept of biosimilar drug was based on and in relation to innovator product. Therefore, the defendant No. 3 is entitled to use the said INN name.

210. It is the admitted position that the regime of biosimilar is new one. It is still to be evolved in this country. Very few approvals have been granted by the Regulatory Authority in new regime. The process of approvals cannot be considered as same in the process of approvals of generic product in chemical form wherein the chemical drug is same where risk is minimum, however, biosimilar/biological drug is not identical.

211. The degree of similarity of the biosimilar drug is maximum to the near of innovator's drug otherwise it cannot be called as biosimilar. The clinical data has to be generated for the purpose of new drug. Thus, heavy burden is upon the Regulatory Authority to examine the clinical trials of biosimilar drug.

212. From the said discussion and overall facts and circumstances, I am clear in my mind that if all the clinical trials have been conducted by the party of biosimilar

drug and all protocols are fulfilled under the Act and Rules and bio-similar guidelines 2012. Under those circumstances, the party/applicant would be entitled to use identical name of INN. Otherwise in failure to do so, the party has to use the said name with certain level of distinction in order to avoid confusion and deception. However, the said name cannot be used or displayed to patients, doctors, hospitals as a brand name. It is to be used to describe its drug only. Any party under the garb of INN name is not entitled to make the misrepresentation or to take any undue advantage, if he does so, he is not entitled to harm the innovator party due to reason that previously INN name was associated with the innovator.

Data Exclusivity

213. On this issue also, both parties have made the same arguments as in CS(OS) No. 355/2014. Still the issue in hand is necessary to be discussed.

214. India has not provided for data exclusivity as a matter of policy which would prohibit defendant No. 3 from making use of data available in public domain, relating to Trastuzumab. The approval of defendant No 3's TrastuRel which is a biosimilar is granted on the basis of comparative data generated with respect to that of the innovator drug.

215. In fact, the WHO Guidelines on SBP's clearly stipulate that the prescribing information should be as similar as possible to that of the reference biologic. The relevant extracts from the WHO guidelines are set out herein below:

"12 Prescribing information and label

The SBP should be clearly identifiable by a unique brand name. Where an INN is defined, this should also be stated. WHO policy on INNs should be followed (http://www.who.int/ medicines/services/inn/ innquidance/ en/ index.html) Provision of the lot number is essential as this is an important part of production information and is critical for traceability in cases where problems with a product are encountered.

The prescribing information for the SBP should be as similar as possible to that of the RBP except for product specific aspects, such as different excipient(s). This is particularly important for posology and safety-related information, including contraindications, warnings and adverse events. However, if the SBP has fewer indications than the RBP, the related text in various sections may be omitted unless it is considered important to inform doctors and patients about certain risks; e.g. because of potential off-label use. In such cases it should be clearly stated in the prescribing information that the SBP is not indicated for use in the specific indication(s) and the reasons why. The NRA may choose to mention the SBP nature of the product and the studies that have been performed with the SBP including the specific RBP in the product information and/or to include instructions for the prescribing physician on how to use SBP products..."

216. The plaintiffs in their pleadings have unequivocally admitted that they do not claim data exclusivity or data protection or have any issue with regard to the use of their publicly available data for the purposes of seeking approval of defendant No. 3's biosimilar product TrastuRel. Herceptin is a public ally available drug and its data relating to test results, dosage, formulations, dosage etc is in public domain. Defendant No. 3's approvals were granted after establishing similarity to Herceptin.

217. Defendant No. 3 has relied upon the Satwant Reddy Report for the interpretation of Rule 122B of the Drugs Rules. Defendant No. 3 has also argued that it is entitled to rely upon and appropriate the plaintiffs' published data entirely without conducting necessary tests to generate data which is to be used in comparison with the plaintiffs' data for establishing biosimilarity with the plaintiffs' Trastuzumab. Counsel for the defendant No. 3 has also referred The Pesticides Management Bill, 2008 and the Intellectual Property Rights Chapter of the TPP Treaty which are irrelevant to the present matter.

218. Counsel for the defendant No. 3 has also informed that in many countries of the world have followed the procedure of biosimilar pathways and data and/or marketing exclusivity for innovator biologics and as details available in public domain and as pathway in place as of today. It is submitted that biosimilar

abbreviated pathways would/can be adopted in India in which there is condition available as of today pertaining to Data Exclusivity for a reference product. The details supplied would show that data exclusivity has been granted for a reference biological product in many countries given as under:

S. No.	Country	Biosimilar (Abbreviated) Pathway in Place	Data/Marketing Exclusivity for a Reference Biological Product
5	Australia	Yes	Yes - 5 years
13	Canada	Yes	Yes - up to 8 years
14	Chile	Yes	Yes - up to 5 years
15	China	No	Yes - The "new drug monitoring period" of up to 5 years only applies to locally manufactured innovative biologics. No marketing exclusivity is available for biological products developed outside of China.
17	Costa Rica	Yes	Yes - 5 years

21	Europe	Yes	Yes - 8 years of data exclusivity and up to 2 years of market
30	Japan	Yes	Yes - A biosimilar applicant cannot be approved until the innovative product on which application relies has completed an eight-year reexamination or post-marketing surveillance period.
39	Malaysia	Yes	Yes - up to 5 years
46	New Zealand	Yes	Yes - 5 years
52	Peru	Yes	Yes - up to 5 years
56	Saudi Arabia	No	Yes - 5 years
57	Singapore	Yes	Yes - up to 5 years
60	Switzerland	Yes	Yes - 10 years

62	Taiwan	Yes	Yes - up to 5 years
66	Turkey	Yes	Yes - up to 6 years
68	Ukraine	Yes	5 years plus 1 year
70	United States	Yes	Yes - 12 years
74	Vietnam	Yes	Yes - up to 5 years

219. The said details provided on behalf of the defendant No. 3 would also show that in many countries data exclusivity has not been granted as per Government policy of respective countries of the world. Similarly the details of bio-similar pathway in place in many countries are given but at the same time the said abbreviation is not possible in few countries of the world. From the said situation in the entire world the respective governments have taken the policy decision. In India, as informed by both sides that as far as data exclusivity is concerned, so far there is no Government policy framed as to whether data exclusivity can be granted to the party whose patent of innovator drug has expired. Similar is the position of pathway/abbreviation of biosimilar products very few approvals have been granted. With the help of so many authorities and intellect involved, while involving Government of India, the biosimilar guidelines of 2012 w.e.f. 15th September, 2012 are placed for the purpose of granting the approvals. However, in the present case, all the defendants addressed their respective arguments by stating that the guidelines are not applicable. As per Rules, the exemption of clinical trials and data of biosimilar product can be granted under sub rule 3 of Rule 1 of the Schedule Y in life threatening and emergency condition in public interest or where the applicant who had already got the approval of the same drug of manufacturing and marketing for several years in India or other countries in case the process of approvals of biosimilar drug is involved.

220. The patent not being for the molecule per se in its unmodified form was not a primary patent. The patent in simple terms was for a mixture of the unmodified molecule. Accordingly, drug manufacturers may manufacture biosimilar versions of

the plaintiffs' Trastuzumab as a consequence of the lapse of the plaintiffs' patent, which drugs should be similar and never identical to the formulation as admitted by the defendants. Patent linkage is not relevant to the issues involved in the present matter since plaintiff No. 1's patent in the plaintiffs' Trastuzumab in India has lapsed. There is no separate legislation to protect the undisclosed test data.

221. The allegations of the plaintiffs against the defendant No. 3 are that they conducted a very limited clinical trial and cannot be permitted to use the data and information for the plaintiffs' Trastuzumab which is publicly available without independently conducting the tests required under applicable law and without complying with the Drugs Act, the Rules or the Biosimilar Guidelines. They cannot rely upon plaintiffs' data in order to misrepresent TrastuRel as biosimilar to the plaintiffs' Trastuzumab.

222. It is the admitted position that the plaintiffs are not claiming data protection for the purpose of comparison of data already in public domain with the data of the applicant at the time of approval. It is also fairly stated on behalf of plaintiffs that the approvals have been obtained on the basis of all clinical trials as prescribed, the plaintiffs have no objection if the correct data available in public domain is used in package insert. However, it is argued that the defendant No. 3 ought to have generated its own data at the time of comparison with the drugs of the parties face to face.

223. In paragraph 1.10 of the Satwant Reddy Report expressly states that "there are a large number of drugs which are mainly biotech drugs e.g. the monoclonal antibodies (MAB) which are clones of a single parent cell and which target sites in the body responsible for diseases like cancer, tetanus and a host of other indications. It is difficult to make generics of such drugs. Although some of Indian companies have succeeded in doing so, yet there is lot more to be done in this area. In case data protection is provided, such categories of drugs may become available early in India as the innovator companies would have greater confidence in entering the Indian market."

224. The report of Satwant Reddy was issued in 2007 when r-DNA products were not included in the definition of 'new drugs' (the definition was amended only in

2011). If it is examined carefully, the interpretation of Part XA of the Drugs Rules in the Satwant Reddy Report is applicable only to new chemical drugs and not biological drugs. As per the Report of the Satwant Reddy Committee, 2007 (the "Satwant Reddy Report"), India does not provide data exclusivity to pharmaceuticals and agrochemicals. There is no separate legislation to protect the undisclosed test data which is submitted to regulatory authorities in case of pharmaceuticals, and proprietary information is protected UNLESS Government of India would take the Policy decision in this regard as in many countries of the world, they took the policy decision respectively i.e. pathways and data and/or marketing exclusivity for innovator biologics.

225. However, defendant No. 3 is entitled to rely upon and appropriate the plaintiffs' published data entirely without conducting necessary tests to generate data for drug in question which is to be used in comparison with the plaintiffs' data for establishing biosimilarity with the plaintiffs' Trastuzumab. Further, while the plaintiffs' data relating to the plaintiffs' Trastuzumab can be used by defendant No. 3 for conducting comparative tests and thereby establishing biosimilarity, such use cannot be extended to misappropriating/reproducing such data in defendant No. 3's test dossiers and/or marketing material. In the present case, in the plaint itself the plaintiffs have given the details in order to show how the literary work has been reproduced by the defendant No. 3 in material form. In the earlier suit, in the unamended plaint, no such claim for infringement of copyright was raised. It was pleaded in the proposed amended plaint.

226. In the present case, the defendant No. 3 is claiming of confidentiality of data relating to the development, testing and approval of drug which is not supported in international practise. In fact, all holders of marketing authorisations for all medicines for human use in the European Union and the European Economic Area are required to electronically submit information on such authorised medicines to the European Medicines Agency and keep such information up-to-date on the online database of the European Medicines Agency in the public domain. Pursuant to the mandate under Regulation (EU) No. 1235 of 2010 of the European Parliament and the Council dated December 15, 2010 amending Regulation (EC) No. 726 of 2014, the marketing authorisation holder's

responsibilities in this regard "include providing all available information, including the results of clinical trials or other studies." The defendant No. 3 time and again refused to give the inspection of the documents as sought by the plaintiffs about the main clinical and pre-clinical tests mainly on the grounds of claiming the confidentiality. Even the defendant No. 3 has filed the application under Section 151 CPC, being I.A. No.25289/2015, during the pendency of hearing of the injunction application seeking the direction permitting the defendant No. 3 to file the documents in a sealed cover and the Registry be directed to place the said confidential documents into the safe custody of this Court and exempt the defendant No. 3 from serving the copies of the documents to the plaintiffs. The reply to the application has been filed.

227. In earlier suit, being CS(OS) No. 355/2014, in paras 133 to 136, after discussion of rival submission, this Court has held and passed the following order:

"133. I have gone through the submissions made by the defendants while resisting the application for discovery of documents filed by the plaintiffs. It appears that the plaintiffs are seeking discovery of the documents so as to prove their case clinically and to provide the infirmities in the defendant's approval process of the drug. The defendant's position while resisting the injunction application has always been that the drug of the plaintiffs is already approved in India and thus data of the plaintiffs and its approval process can come in aid of the defendant while seeking its approval of the drug BMAB 200 based on referenced biologic.

134. If this position taken by the defendant No.2 qua the data and approval of the plaintiffs' drug by calling it a public ally available documents, it is beyond comprehension as to how the defendant No.2 after submitting the documents with defendant No. 1 can call their documents as confidential in nature. The defendants' stand is surprising when they go on state that the plaintiffs cannot also inspect the documents from the office of the defendant No. 1 as it is hotly contested matter. Off course, there is an attempt to withhold the documents from the plaintiffs who are the aggrieved parties whose product is referenced against by the defendant No.2 who cannot withheld the documents which would only reveal whether the requisite and crucial trials have been conducted by the defendant

No.2 or not. There is no force in the submission of the defendant No.2 that since the original record is submitted by the defendant No. 1, the Court may examine the same. As a matter of fact, the plaintiffs' assistance on this issue is required in order to find out the truth.

135. Under such circumstances, I do not find any impediment in allowing the application seeking discovery of the documents in as much as the moment the approval has been allowed, the document submitted before the defendant No. 1 can be examined by the plaintiffs being aggrieved party. However, in order to strike the balance between the parties and concerns raised by the learned counsel for the defendant No.2 about confidentiality of the document, it would be proper that let the documents as mentioned in the application be filed in sealed cover within two weeks from today. The same be kept in safe custody of Registrar General. Two lawyers and an expert from the plaintiffs side would inspect the said documents in the presence of two Advocates from the side of defendant No.2. They (members of club) would be bound by confidentiality and shall not make copies or disclose the contents of the said aforesaid documents to anyone, oral and written communications to the press, blog publications etc. in order to maintain the confidentiality except in the present proceedings. The inspection can only be done through the confidentiality club members and no copies will be made of such confidential documents. After the inspection, the aforesaid confidential documents, the same be resealed and again deposited with the Registrar General of this Court. After inspection, the plaintiffs would be at liberty to amend their pleadings if so required.

136. The application is accordingly allowed in terms as mentioned above."

228. Thus, there is no force in the prayer in the application, being I.A. No.25289/2015, filed by the defendant No. 3 under Section 151 CPC. The same is accordingly dismissed. The defendant No. 3 in the present matter also to comply the same direction in terms of para 135 of the order passed in CS (OS) 355/2014, as mentioned above.

229. The reliance of decision under The Pesticides Management Bill, 2008 would not help the case of the defendant No. 3 in view of the nature of drug involved in

the present case is for cancer. The said principles cannot be applied in the present matter.

230. After having considered the arguments of the parties, I am of the opinion that unless Government of India frames policy to declare as to whether after expiry of patent, the data in public domain can be used as pathways or not, the regulatory authority can neither disclose nor rely upon the first applicant's data at the time of granting marketing approval to the subsequent applicants. It is for the Government to decide that such protection for certain fixed period to the innovator should be granted or not.

Have Guidelines 2012 been followed in the present case?

231. Now, I shall advert to the facts of the present case and evaluate the contention as to whether guidelines can be said to be inapplicable merely due to the reason when those were applicable with effect from 15th September, 2012, the process of clinical trials was already commenced or the committees framed under the rules to bypass the guidelines on that basis and proceed to grant the approvals on the premise that the guidelines are non est.

232. Defendant No. 1 in its Written Statement has contended that the Biosimilar Guidelines 2012 are not statutory in nature as the clinical trial protocol in relation to the defendants' drug had been approved prior to the publication of the Biosimilar Guidelines. The stand of defendant No. 3 is two-fold; firstly it is alleged that the guidelines as such are not applicable and secondly, it is stated that the approvals obtained by the defendant No. 3 are in accordance with the Act and Rules and rather the biosimilar guidelines of 2012 provide a regulatory pathways for approval. However, the stand of defendant No. 1 remains the same as in earlier suit, being CS(OS) No. 355/2014. It is reiterated in the written statement that these are not statutory.

233. On this issue, the defendant No. 3 has argued against the arguments addressed by defendants in earlier suit filed against the different defendants. In this case defendant No. 3 has alleged that it complied with all the parameters of the Guidelines as given below:

a) Similarity with respect to quality (physicochemical, structural, purity and potency) proven to reference biologies

b) Similarity with, respect to preclinical assessment (toxicity studies) proven to reference biologic

c) Similarity with respect to clinical assessment (Safety and Efficacy) proven to reference biologic

d) Data from each of these studies were reviewed in details by the RCGM and upon satisfactory review necessary approvals were given.

234. The alternative plea is taken that the guidelines were not in force during the period from 2009-2012. The process followed is almost identical to the Guidelines of 2012. The defendant No. 3 submits that the process of development and approval of the defendant's drug had commenced in 2009 itself and hence the Guidelines do not strictly apply.

235. It is stated in the reply that the 2012 Guidelines itself create a distinction between a New Biological Entity and a Similar Biologic. The Guidelines state that if comparability to the reference product is demonstrated then a reduction in data requirement for pre-clinical and clinical studies is possible. It is seen that the 2012 Guidelines on Similar Biologics provides a pathway whereby the pharmacokinetic studies; which are primarily the motive for conducting Phase I trials, may be conducted either in healthy volunteers or in patients, whereas Phase III studies are conducted on patients. As there is already publicly available data of the pharamacokinetic studies in healthy volunteers in the form of Global Phase I studies, for a biosimilar cancer drug, generally the developer conducts pharmacokinetic studies on patients without repeating such studies on healthy volunteers using cytotoxic cancer drugs.

The 2012 Guidelines on Similar Biologies under clause 8.2 convey a pathway that the PD studies may be combined with PK studies. PD can also be a part of Phase III trials wherever applicable. A similar facility is even permissible under Schedule Y2(8)(iii) of the Drugs Act.

236. No doubt the defendant No. 3 was still conducting clinical trials of its product when the Biosimilar Guidelines were issued in the year 2012, However, the alteration in the regulatory framework by passing of the guidelines during the pendency of the application of the grant of the approval for manufacture does not allow the defendant No. 1/ DCGI to overlook the guidelines which already came into force by 15th September, 2012. This is due to the reason that the defendant No. 1 was still in sesin of the application for the grant of the approval and being a functionary under the Act and the rules framed thereunder considering the object which was sought to be achieved by the guidelines which was to ensure the safety, efficacy of the medicines in relation to complex compounds involving biologics, the defendant No. 1 was obligated to take into consideration those guidelines passed by CDSCO of which the defendant No. 1 was part at least, it was the duty of defendant No. 1 to bring to the notice of the Committee about the guidelines.

237. Even nothing is available on record to suggest that the guidelines have been followed or if the same are ignored or some speaking orders are passed. Rather record discloses that when the request of all the clinical trials of Phase III was submitted the guidelines of 2012 were already in place. The recommendation of approvals was granted on 7th May, 2015 and the approvals were granted on 2nd June, 2015. It is pertinent to mention here that the defendant No. 3, who is a private party in the present case cleverly taken the stand that the guidelines have been followed as it was aware that in earlier suit, the private party on this aspect was on very week footing. In fact the defendant No. 3 has taken the alternative plea, however, the defendants No. 1 and 2 have not specifically either pleaded in the written statement or argued before Court that all the approvals are granted after following the Guidelines 2012 or the record submitted disclosed.

238. Even the Mashelkar report, which the defendants rely heavily to contend that the system of approval, was already in place and there was no deviation done by the defendant No. 1 while granting the approval, also provide for the conducting of the clinical trials in phases and mandate for 90 days period for analysis of the clinical trial data and response thereon by the defendant No. 1 and the committees formed under the rules. Thus, the defendant No. 1/ NDAC on receipt of the clinical

trial data of the defendant No. 3 on 25th March, 2015 (without having clinical trial results of phase I and phase II) could not have abbreviated the said phases without giving any reason. The recommendation was made in less than 90 days i.e. within 41 days even when there are three attendant circumstances which are staring on the face of the defendant No. 1 that being; first is the time period provided by the expert report Mashelkar report providing the period of 90 days time to analyse the said data relating to clinical trial; second is the notification of the guidelines on similar biologics on 15th September, 2012 providing for the additional requirements keeping into mind the safety and efficacy of the medicines and also insisting on the conducting of the clinical trials and third is that the defendant No. 1 was made aware by the time about the scheme of bio similar products while being a participant to CDSCO guidelines that the regime of bio-equivalence is totally distinct from that of the bio similar and thus the approval for the manufacturing of the drug based on similar biologic cannot be granted by merely demonstrating the similarity between the two compounds as done in bio equivalent but it requires demonstration of similarity in other terms as indicated in the guidelines.

239. In this backdrop, when the defendant No. 1 was already made aware of these circumstances, in the absence of any special reasons given by the defendant No. 1 to be recorded in the writing in relation to the exemption of the requirements of the guidelines or the requirements to conduct the clinical trials in three phases.

Under Clause 6.3.2 of the Biosimilar Guidelines complete characterisation studies for similar biologies, including physico chemical characterisation studies, biological activity, immunological properties, functional assays, purity, contamination, strength and content is required. The explanation given by the defendant No. 3 is that Biosimilar Guidelines are not applicable is hence not acceptable. The stand of defendant No. 1 that those are not statutory is contrary to the scheme of the Act and Rules as well as the spirit of guidelines of 2012 framed by the Government.

240. It is a matter of record, on one hand the defendants are arguing that the clinical trials of Phase I and Phase II are not required and guidelines of 2012 are not applicable, and on the other hand, they are canvassing that most of clinical

trials applicable to Phase I and Phase II have been combined with Phase III. If these are combined with Phase III trial, why those Phase and Phase II trials are not registered by the defendant No. 1 as admitted.

241. The perusal of the guidelines of 2012 would show that no doubt that there exists a provision for the reduction in the requirement of the clinical data in the approval process of the bio similar product on the basis of the reference biologic. However, to counterbalance the same, the similarity with the referenced biologic has to be establish not merely in the manner of bio-equivalence regime but also on other facets as well. There are provisions for the product characterisation provided in detail for the purposes of the studies wherein similarities and characteristics of similar biologic has to be seen and examined on various facets including structural and physicochemical properties, biological activities, purities and impurities etc. Likewise, for the clinical trial application, there are additional requirements which have been provided which are mentioned in para 6.2 of the guidelines.

242. From the reading of the guidelines holistically, it can be said that besides establishing the similarity on the several counts, the guidelines also lays great stress on the quality comparability studies, process parameters, comparability of manufactured product at clinical scale. Further, the comparative clinical trials are essential in order to ensure safety and efficacy of the similar biologics. The said clinical trial/ study analysis should spent sufficient amount of time so as to see the effects of the same on substantial number of patients in order analyse the similarity and difference between the similar biological product vis-a-vis the referenced product as per the paragraphs of the guidelines. Some of the excerpts of the guidelines are reproduced below:

Comparative clinical trials are critical to demonstrate the similarity in safety and efficacy profiles between the similar biologic and reference biologic with few exceptions (e.g. recombinant human soluble insulin products for which only comparative clinical safety study is required). The design of the studies and the clinical comparability margins of the primary efficacy endpoints are important and should be given careful consideration and should be justified on clinical grounds. In line with the principle of similarity, equivalence trials with equivalence designs

(requiring lower and upper comparability margins) are preferred. If non-inferiority trials are required they must be clearly justified and applicants are advised to consult with CDSCO prior to study initiation. Sample sizes should have statistical rationale and comparability limits should be defined and justified prior to conducting the study.

The nature, severity and frequency of adverse events should be compared between the similar biologic and reference biologic and should be based on safety data from a sufficient number of patients treated for an acceptable period of time. Efforts should be made to ensure that comparative clinical studies have a sufficient number of patients treated for acceptable period of time in order to allow detection of significant differences in safety between similar biologic and reference biologic.

(Emphasis Supplied)

243. If there are number of aspects which have been highlighted as a matter of studies to be done prior to the grant of the approval including the product characterisation, comparability on the clinical trials, quality comparability studies and there are additional requirements for conducting the clinical trials with the importance of the same being underscored, the question to be asked is can we really say that the said process be compromised/ overlooked by proceeding to totally exempt the clinical trial route and solely on the ground that the drug has already been approved in India in favour of the plaintiffs which is the substratum of the argument of the defendants. These are the reasons why the guidelines are to be read in conjunction with the Drugs and Cosmetics Rules and in case the aim of the guidelines are to achieve the safety, quality and efficacy of the similar biologic drug so that public get the safe medicine.

244. But in the present case, the stand of defendant No. 1 is that the guidelines of 2012 are not statutory. On the other hand, the defendant No. 3 is not prepared to give the inspection the documents pertaining to comparative clinical trials and studies to the plaintiffs wherein similarities and characteristics of similar biologic is to be addressed.

245. The defendants in the present case have taken the inconsistent position as the defendant No. 1 and Biocon Limited have argued in earlier suit C.S.(O.S.) 355/2014 that the Biosimilar Guidelines are not statutory in nature. However, in the present case, defendant No. 3 has admitted the applicability of such guidelines and relied on them to justify the process of approval of TrastuRel, particularly the provisions in relation to extrapolation of data to the Additional Indications. Even defendant No. 1 has tried to justify the grant of approval for the Additional Indications as permissible under the Biosimilar Guidelines.

246. The explanation of the defendant No. 3 is that all the trials have been exempted by the defendant No. 1 and various committees and even the plaintiffs are not entitled to inspect the said documents after approvals, as the defendant No. 3 is claiming confidentiality of those documents. The said stand by the defendant No. 3 cannot be accepted as on one hand, the defendant No. 3 is alleging and insisting to use the data, references and name of the plaintiffs in order to claim biosimilar drug, on the other hand, they do not want to give inspection of documents of characterisation and comparability on the clinical trials and address their arguments before the Court.

247. The defendant No. 1 is admittedly serving a public purpose under the Drugs Act and is responsible for public safety, it is imperative for the defendant No. 1 to ensure that drugs approved by it have been adequately tested before such drugs are introduced in the market.

248. Therefore, assuming that the defendant No. 3 might have undergone the onerous processes of the seeking many approvals, but that by itself does not ipso facto allow the defendant No. 3 to contend that the norms and requirements framed under 2012 guidelines are fulfilled already.

249. The defendant No. 1 and the authorities/ committees framed therein ought to have taken into consideration the guidelines when they were having time to analyse the clinical data as per the existing rules and could have also recorded the reasons for granting the specific exemptions as contended by the defendant No. 3 before this court if so claimed by the said defendant and could not have straightaway proceeded to grant the approval to manufacture biosimilar products

by completely overlooking the guidelines and the requirements to conduct the clinical trials which were aimed to ensure the safety, efficacy and quality of the medicines based on similar biologics.

250. In my analysis, given the distinct nature of the guidelines framed and object sought to be achieved by them, the argument of the defendant No. 1 and defendant No. 3 that the Appendix IA is applicable in the case of the defendant No. 3's drug and that is the reason for the abbreviated information being provided and prompt approval is granted suffers from fundamental flaw/ infirmity which no reasonable person who is made aware of the guidelines of 2012 already would undertake unless there is total non application of mind or other extraneous consideration.

251. It appears prima facie that the defendant No. 1 has ignored the significance of the primary end-point of different phases of clinical trials there is no overlap of primary end points of the four phases of clinical trials and, as stated in paragraph 8.3 of the Biosimilar Guidelines, "primary efficacy endpoints are important and should be given careful consideration and should be justified on clinical grounds."

252. The combining/skipping various phases of clinical trials is not justified as it would render redundant the underlying logic of sequential testing vis-a-vis primary end-points, target population and sample size. Paragraph 7.3 of the Biosimilar Guidelines clearly provides that the RCGM recommends the required phases of clinical trials based on an assessment of the pre-clinical test results, paragraph 10 of the Office Order issued by the Department of Biotechnology bearing No. BT/BS/17/175/2005-PID and dated January 2, 2006 wherein the RCGM recommended that all four phases of clinical trials should be undertaken. The defendant No. 1 does not have expertise to analyse the pre-clinical (animal study) reports and draw conclusions. RCGM is the appropriate authority for this purpose.

253. I do not agree with the submissions of the defendants that since Biosimilar Guidelines of 2012 are prospective and not retrospective therefore defendant No. 1 was not obliged to apply the same guidelines when the approvals granted as the defendant No. 3. The relevant date for application of guidelines is of 2012, the date of approvals is the main date. In the present case, the date of approval was

granted on 2nd June, 2015 when the Bio-similar Guidelines of 2012 were in force.

254. I also do not agree with the defendant No. 3 that the said Guidelines do not state explicitly that the Guidelines or specific requirements under the Guidelines are applicable for ongoing clinical trials as on the date it became effective because of the reasons that most of the meetings held after the guidelines were inoperative at the place. The safety and efficacy cannot be put at risk because there may be chances of lack of rigorous trials on crucial safety and efficacy parameters before a life saving drug is launched in India. It is mandatory that process of approval of bio-similar should be more stringent and rigorous than for other non-schedule drugs or generic drugs/chemical drugs.

255. Hence, it is the obligation of defendant No. 1 to consider the Guidelines of Biosimilar same on the date of approval as it is a matter of life and death of a patient(s) in case the approval is granted contrary to rules and guidelines even those may not be mandatory in nature.

256. As per the Drugs Act and the Biosimilar Guidelines envisage that all phases of clinical trials are required to be conducted by a drug manufacturer unless a particular phase is exempted in accordance with applicable law. As such, neither the RCGM nor the DCGI can permit the defendant No. 3 to abbreviate the clinical trials' procedure outside the purview of this legal regime unless the requisite test is exempted or reduction of data as per Guidelines 2012 of biosimilar product. Such thing has not happened in the present case.

257. Prima facie, there is no objective satisfaction recorded by the defendant No. 1 which provide for any reason for dispensing with the requirement of conducting of the clinical trials of Phase I and phase II and even if as on the date of the grant of the permission to conduct phase III trial directly, the guidelines of 2012 was not in force, still even on 27th March, 2015 when the defendant No. 1 had forwarded the results of the Phase-III clinical trials to the NDAC by the defendant No. 1 requesting for expert opinion as to whether defendant No. 3 can be considered for granting marketing authorisation, the defendant No. 1 or the expert committee on the said date or thereafter on subsequent dates when the matter was forwarded to further committees, the said bodies including defendant No. 1 ought to have

further clarified for the requirements of conducting the clinical trials of all the phases or in the alternative asked for the reasons and justifications for not doing so once the contrary position is emerging from the guidelines on biosimilar products of 2012 and they were already in place and in effect if so desired should have passed the orders on the requirement of the reduction of the data submission in the appropriate case or should have insisted for the requirements or material in terms of the guidelines, none of the resources have been indicated or adopted by the defendant No. 1 or expert bodies who were all aware of evolution in this field of science and developments in the policies in the form of guidelines on biosimilar products.

258. Therefore, the prima facie, the approval granted by applicability of the second proviso to rule 122 B read with Appendix IA on the basis of the generic medicine cases is on the face of it in contravention of the guidelines without even looking at the additional requirements provided therein to conduct the studies therein by the applicant like the defendant No. 3 herein.

259. Obviously, when such circumstances were existing, the defendant No. 1 had to deal with the situation with the extreme level of sensitivity and care so that the due process is following while granting the approval which has been on the face of it has been flouted and bypassed in the present case. Therefore, I do not agree with the submission of the reasonableness as canvassed by Mr. Jain, learned ASG appearing on behalf of the defendant No. 1. In the present case, the process followed is flawed and suffers from the vice of the non application of mind and non adherence of the statutory provisions of the Act and Rules as well as Biosimilar Guidelines of 2012 by the defendant No. 1 who itself to watch not merely in the private interest but also public interest. There are many lapses, procedural impropriety and the approvals are granted in illogical manner.

260. Considering the overall facts and circumstances, I am of the considered prima facie opinion that the defendant No. 3 has not obtained the approvals as per existing protocol of biosimilar drug. The same are contrary to the Rules and Guidelines of Biosimilar 2012. As per the case of defendant No. 1 that guidelines are not in statutory and remaining defendants have canvassed that those are not

applicable, the said arguments are wholly baseless and rejected, thus, the approvals which are in the hands of defendant No. 3 granted about the drug manufactured and marketed by the defendants No. 3 are not in accordance with the protocol of biosimilar drug and guidelines, so far the defendant No. 3 has not been able to satisfy before the Regulatory Authority as to whether the drug manufactured and marketed by the defendant No. 3 is biosimilar. It appears that the procedure adopted and applied in the present case by the defendant No. 1 and other authorities and committees is akin to the procedure of granted the approval of bio-equivalent drug which is quite distinct from the scheme of granting the approval of biosimilar drug, the same is not correctly examined by the Regulatory Authority as to whether tests in the present case are conducted were adequate or inadequate in compliance with applicable law. No doubt as per guidelines under various provisions, the regulatory authority's committees are empowered to apply pathway of abbreviation for bio-similar drug ban the unfortunate part of the matter is that guidelines have not been considered. The power to suspend/cancel the approval about the noncompliance lies with the Licensing Authority under Rule 122 DB.

261. In view of discussion held and prima facie findings arrived by me, the question now arises as to whether the plaintiffs are entitled to any interim relief in the form of injunction as prayed for in the application. The plaintiffs have number of grievances with respect to the market approval granted to the defendant No. 3. The said grievances include that the defendants product claiming to be biosimilar as that of the plaintiffs' drug bearing the trademarks HERCEPTIN, HERCLON or BICELTIS and use of the data of the plaintiffs drug, use the INN name and use the bio similar drug as a word to attract the customers in the course of the trade. I have already arrived at certain prima facie findings wherein it has been observed that the defendant No. 3 products have been granted approval without adherence to the guidelines of 2012 and also on the premise that the scheme of the bio-equivalence is akin to bio similar when it is in fact not so. In this backdrop, it is to be really looked into as to whether it would be befitting to altogether prevent the defendant No. 3 to manufacture and market by launching TrastuRel drug involved in the present case and if not then to what extent the interim protection can be moulded so that pending the final decision on the validity of approval before this

court (which the defendant No. 3 already possesses) on the adherence of the guidelines, the interests of both the parties are not affected and simultaneously the public interest is equally upheld.

262. I am of the view that the approvals granted to TrastuRel product are not on the basis of the adherence of the Guidelines of 2012 and rules framed under the Drug Act. The final finding in this respect is yet to be arrived after the present suit is heard upon completion of the trial. Pending the final outcome of the suit, there is a need to arrive at interim measure by working out certain terms between the parties by passing the following directions:

a) The defendant No. 3 may launch to manufacture, market and advertise their product under the name TrastuRel on the basis of the approvals already granted to defendant No. 3 without calling their product as "bio similar" and/ or "bio similar to HERCEPTIN, HERCLON, BICELTIS" or in any way ascribing any bio-similarity with that of the plaintiffs products HERCEPTIN, HERCLON, BICELTIS in any press releases, public announcements, promotional or other in printed form and from relying upon or referring the plaintiffs' names.

b) The defendant No. 3 may also manufacture and market the drug by qualifying the INN name Trastuzumab but not to use the said name stand alone on the carton or package insert as a brand name. The defendant No. 3 can use the INN name as Reliance Trastuzumab or TrastuRel wherever applicable to describe the composition of molecule on the product as well as in its insert and not in a prominent manner. The said expression shall be used at the bottom part of the carton and should be in small size letters than the brand name TrastuRel.

c) In view of prima facie findings that the use of the data by the defendant No. 3 in the product insert without undergoing the entire process of the trials is misleading, the defendant No. 3 is also restrained from using the data relating to manufacturing process, safety, efficacy and tests conducted for the safety of the drugs as complained of by the plaintiffs till the time the final decision on the issue of the bio similarity is made in the present suit.

d) In the event, the defendant No. 3 intends to claim bio similar as a description of its product or part of its promotional campaign or otherwise in any other form, the defendant No. 3, if so advised, can reapply the said license before the relevant authorities including defendant No. 1 and in which case, the defendant No. 1, the authorities and committees framed therein shall decide the said approval application in accordance with the Rules and Guidelines of 2012 and also the observations made by this court in the present order. The defendant No. 3 shall also be entitled to use the data of the plaintiffs for the comparison purposes before the Regulatory Authority. In the alternative, the defendant No. 3 may await the outcome of the present suit and can continue with the present arrangement as an interim measure.

e) This interim measure is made only in view of the peculiar facts in the present case only wherein the defendant No. 3 is already in possession of approvals granted rightly or wrongly validity of which is questioned in this suit. In future application for approval(s) of biosimilar shall be decided by the defendant No. 1 and authorities and committees while considering the guidelines of 2012 and also the findings arrived at in the present order by this Court as well as strictly as per the provisions of the Act and Rules.

263. The findings made herein above are all tentative in nature and shall have no bearing when the main suit would be decided after trial on merits.

264. Both the above mentioned applications are accordingly disposed of.

265. No costs,

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266. List on 2nd June, 2016 before the roster Bench.