The different stages of the process exhibited in figure 1 show the registration of a patent application regarding certain chemical entities at a time 0 and the market authorization at ca. 10 years. At this point it should not be left out of sight, that the filing of a patent application is preceded by a time of basic research directed towards the identification of a suitable biological target for a given disease followed by the identification and first round of optimization of chemical compounds which are suitable for the purpose (e.g. inhibiting a metabolism, a viral action, bacterial growth etc.). This time may conservatively be estimated to range from 1 to 3 years, depending on the complexity and the novelty of the biological target.[15] During the phase of preclinical development, several of such optimization cycles are usually being run through until candidate compounds which are suitable for Phase I clinical trials are available. While the expenditures of the Preclinical Phase may already be significant (depending on the disease models available, some viral diseases can for example only be studied in primates), the clinical phases do exceed them several times. As part of the preclinical development of a drug candidate, toxicology and safety studies as well as studies regarding suitable pharmaceutical formulations and the stability are being carried out. Many compounds fail already in this stage, as they might have a desirable activity profile, but turn out to be also toxic. While an early understanding of the interactions with other drugs is desirable, such studies are oftentimes not being carried out before the completion of Phase I clinical trials.[16]

B. New Drug Approval Regulations

The European system offers three routes for the authorisation of medicinal products, the so-called centralized procedure[17] using the

15 Authors own experience from drug research in various pharmaceutical companies.

16 EMA, *Guideline on the Investigation of Drug Interaction*, (Apr. 22, 2010) http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/05/WC500090112.pdf, at 7 (last visited Aug 2, 2012).

17 Regulation (EC) 726/2004, 2004, O.J. (L 136) 1.

EMA, the mutual recognition procedure[18] and the decentralized one.[19] The decentralized procedure (DCP) for medicinal products, which have not been authorized before in any member state, allows for the marketing authorisation application to be submitted simultaneously in several Member States, one of which acts as the reference member state and coordinates the process. At the end of this procedure national marketing authorisations are granted in all the Member States involved. If the medicinal product has already been granted a marketing authorisation in one of the EC member states, then the mutual recognition procedure (MRP) is used.[20]

Article 3 and the Annex of the Regulation[21] define the types of products which fall within the scope, in particular article 3(1) and the Annex define the medicinal products for which the centralized procedure is mandatory.[22]

C. Generic Drugs Approval.

As far as generics are concerned, pre-clinical tests and clinical trials are not necessary if it has been demonstrated that the generic product has "the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product[23], and whose bioequivalence with the reference medicinal

18 Regulation (EC) 764/2008, 2008, O.J. (L 218) 21.

19 Directive (EC) 2004/27, 2004, O.J. (L 136) 34.

20 EMA, *EMA procedural advice for users of the centralised procedure for generic/hybrid applications*, http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004018.pdf (last visited March 5, 2012).

21 *Supra* note 17.

22 *Supra* note 17, Art. 3(1) and Annex.

23 Art. 10(1) and Art. 10(2)(a) of Council Directive (EC) 2004/27/EC of 31 March 2004, OJ L 136, 34, 39 (2004): "Reference medicinal product shall mean a medicinal product authorised under Article 6, in accordance with the provisions of Article 8", and "which is or has been authorised under Article 6 for not less than eight years [Data exclusivity 8+2 market exclusivity +1 for new indication] in a Member State or in the Community".