as well as recommendations for the extent of testing. The OECD guidelines on testing methods[1] give recommendations on experimental details such as minimum animal numbers and parameters to be tested as well as reporting of the results, which can also be applied for drug testing. In addition, there are specific guidelines for pharmaceuticals, most important being the ICH guidelines[2] addressing safety aspects, quality aspects (e.g., assessment of impurities), as well as multidisciplinary aspects. In addition, there are regional guidelines, e.g., those published by EMA[3] and FDA[4], also covering aspects not addressed in ICH guidelines. The regulatory safety testing has generally to be performed according to good laboratory practice (GLP), which includes testing in a test facility certified for the specific GLP studies and using test material according to GLP standards.[5]

For the nonclinical safety assessment in the process of drug screening and drug candidate selection, there are no formal regulatory requirements, neither with regard to the type of testing to be performed nor with regard to the quality of such data. As a consequence, the screening program is generally designed to support the choice of the best candidate by early identification of important development hurdles. There is a lot of space for tailor-made approaches based on the target, the chemical class of compounds, the intended therapeutic indication, and also the previous experience within these mentioned fields. The extent of screening largely depends on the need for differentiation between candidates as well as the need for early de-risking of specific liabilities. There are some areas, which are responsible for a high attrition rate and for which methods are available allowing for high throughput. Thus these endpoints are often recommended to be included into an early screening cascade prior to start of lead optimization. Examples for such endpoints are cytotoxicity (EC_{50} of cytotoxicity on nontarget cells vs. EC_{50} of primary pharmacodynamics effect on target cells), mutagenicity, and hERG current inhibition or hERG binding. For follow-up candidates, additional toxicity screening may be included depending on the nature of the findings with previous front-runner compounds. Examples for such additional screening are phospholipidosis and mitochondrial toxicity (Kramer et al. 2007). At the stage of candidate selection, in vivo pilot toxicity studies are still state of the art to derive the most predictive data for later preclinical and clinical development.

As mentioned above, the preclinical development program for the preparation of the initial clinical trials (FiM: first in man) is set forth in regulatory guidelines. The focus in the following sections will therefore be an overview of most important

[1] http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788

[2] http://www.ich.org/home.html

[3] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000397.jsp&mid=WC0b01ac058002956f

[4] http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

[5] http://www.oecd.org/chemicalsafety/testing/oecdseriesonprinciplesofgoodlaboratorypracticeglpandcompliancemonitoring.htm