TECOmedical Group

Biomarkers – an indispensable tool for drug development

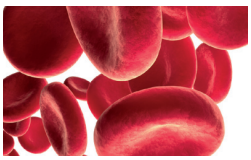
Our contribution as specialist in biomarkers and biosafety.

Custom Assay Development

Project Management

Kidney & Liver Toxicity





Blood Product Safety

Drug Efficacy

Cell Death

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Genotoxicity

Environmental Toxicity



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Metabolic Syndrome

THE biomarkers CONSORTIUM

Immunogenicity

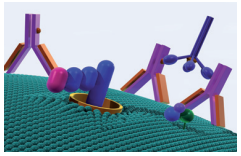
Hemocompatibility

Pharmacokinetics & Pharmadynamics



Bone & Cartilage

Complement Activation



REDOX Potential Oxidative Stress

always your partner

Biomarkers – an indispensable tool for drug development

Professional Project Management & Consultancy

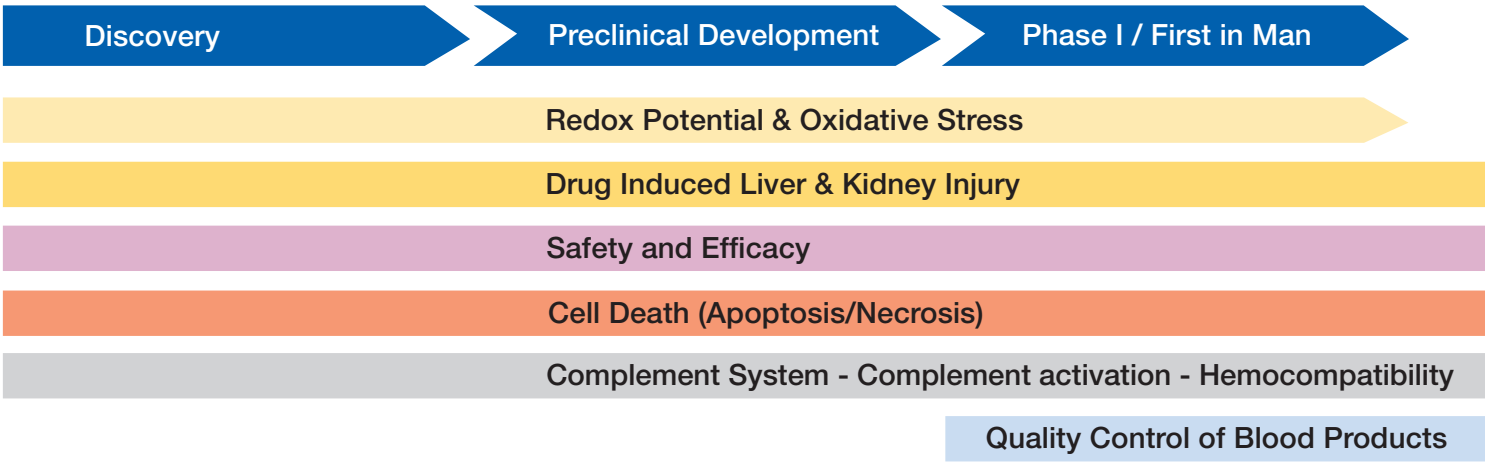
TECO project management follows a strict R&D process, milestone reporting, customer authorization for each phase, training and technical support to ensure successful development and transfer of technology. We have senior project managers in our team have gained in-depth ex-perience in preclinical, clinical development and manufacturing in SME and leading pharma companies such as Amgen, Merck-Serono, Novartis, and others. Our project managers accompany not only TECO's internal assay development but can be engaged to drive your internal projects. They have know-how and proficiency in the various disciplines including regulatory affairs required for drug development.

Redox Potential & Oxidative Stress

Oxidative stress is an imbalance between oxidizing and reducing agents, hence is involved in the pathogenesis of various diseases. The novel test system determines the redox potential in biological samples in two ways:

1) Static ORP (sORP), a “snapshot” of current redox balance, correlating to illness;
2) Capacity ORP (cORP), assessing antioxidant reserves, correlating to the ability to manage illness or injury.

sORP and cORP assays allow the easy assessment of the redox potential of drugs in (pre-) clinical and safety studies.



Custom Assay Development

To mitigate resource constraints TECO offers tailor-made ELISA assay development to support manufacturing and (pre)clinical studies. Using our long term experience as diagnostic company with more than 15 years on the market we offer you our platform technologies (antibody generation, purification, labelling, etc.) and manufacturing capabilities to develop and produce the tests you need. Highest quality is ensured by ISO 13485 certified QMS and stringent QC processes. Our specialities:

- Impurity assays (e.g., Host Cell Protein, protein A), ELISA development and testing for biologicals;
- Anti-Drug Antibodies (ADA) and confirmatory assay development to monitor potential onset of immuno-genicity;
- Pharmacokinetic and pharmacodynamic assays in addition to our broad test portfolio.

[Guidelines: ISO 13485]

Drug-Induced Liver & Kidney Injury

Drug-induced liver injury (DILI) is a leading cause of liver failure and transplantation. Consequently, the early identification of drugs causing toxicity of the liver and /or kidney is an important safety aspect during drug development and can help to reduce the risk for the patient and failure of new medicines. The European Innovative Medicines Initiative (IMI) recently validated liver and kidney injury biomarkers with a consortium of participants from the pharmaceutical industry and regulatory bodies. Among those biomarkers caspase-cleaved and uncleaved Keratin 18 (M30 and M65 assays) and the Liver&Kidney bio-marker α-GST demonstrated in 2D and 3D models to be most useful for the prediction of DIKI and are therefore acknowledged by regulatory agencies as concomitant tests upon drug development.

- DILI: Letter of support for drug-induced liver injury (DILI) biomarker, 30 September 2016, EMA/423870/2016 and FDA July 25, 2016.
- DIKI: Letter of support for drug-induced renal tubular injury Biomarker(s),14 December 2016

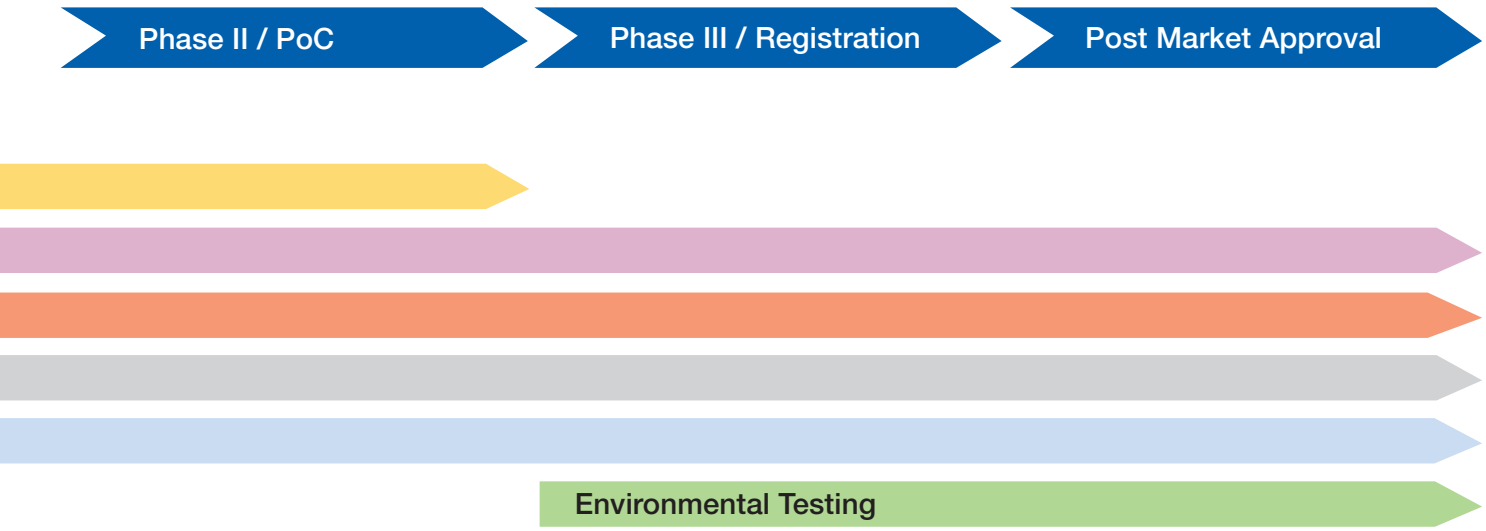
Complement System

Testing of complement activation is mandatory in (pre)clinical and safety studies with medical devices, radiocontrast agents, nanomedicine candidates, including:

- Hemocompatibility – e.g. for medical devices and blood products
- CARPA – Complement activation-related pseudoallergy caused by i.v. administered drug carrier systems (liposomes, micellar drugs, polymeric or polymer coated/conjugated nanoparticles), radiocontrast agents or biologicals (monoclonal antibodies, other protein therapeutics)
- Complement-Dependent Cytotoxicity (CDC) (e.g. therapies with cytotoxic biologicals)
- Complement-targeted drug discovery (e.g., complement inhibitors)
- Complement system as enhancer of therapy (e.g., monoclonal antibody therapy)

TECO provides (pre)clinical Complement assays and procedures for hemocompatibility of medical devices and blood products, as well as for drug safety and efficacy testing, fulfilling the regulatory guidelines

[Guidelines: ISO 10993-4 (2009); ASTMF2567; ASTMF2065; ASTMF]



Safety Testing

Drugs approved must be safe meaning that the benefits of the drug appear to be greater than the known risks (side effects) and effective. Side effects can vary from minor problems to life-threatening events, such as an increased risk of a heart attack.Testing for possible side effect's takes place during the drug development process in the pre- and clinical phase, e.g.

- NT-proANP as biomarker of cardiac hypertrophy in preclinical(rats) and clinical toxicology investigations
- FGF-23 for monitoring of potential disorders of the phosphate metabolism in the context of intravenous iron replacement therapy.

Efficacy Testing

Efficacy is the drug 's capacity to produce a desired effect. A drug should be applied only when it will benefit a patient. Benefit takes into account both the drug's ability to produce the desired result (efficacy) and likelihood of adverse effects (safety). Efficacy biomarkers can be used in cell culture, animal models or human clinical trials to assess the drug's ability to produce the desired results, e.g.

- Keratin18 (M30 and M65 assay) is used for measuring a drug's capacity to cause apoptosis of cancer cells.
- A significant decline in Pro-Insulin levels are indicative for the drug's capacity to reverse diabetes Type 2.

Cell Death - Anti-Cancer Agent testing

Many modern cancer treatments including therapeutic monoclonal antibodies, involve cell death (apoptosis/necrosis). Drug efficacy of new candidates and drugs in development may be screened in cell culture, 2D and 3D tumor models, animals as well as in patients using epithelial cell death markers - caspase cleaved (M30) and un-cleaved (M65) fragments of Keratin 18.

M30 specifically identify compounds that induce apoptosis, a major target of anti-cancer drugs. M30 & M65 describe the relative contribution of apoptosis and necrosis, only a single, specific time point is required because the accumulation of intact and cleaved K18 is detected. Combining both tests is helpful to proof and study the mode of action of new chemical and biological entities.

Quality Control of Blood Products

Fractionation of human plasma used for the production of human albumin and immunoglobulins harbours the risk of concentrating Prekallikrein Activator (PKA). Administration of high levels of PKA is a safety concern as it can lead to the increase of kallikrein and cause a shock in the patient. Therefore, all manufacturers are requested to measure PKA levels in each batch of final blood products upon release.

The PreKallikrein Activator Assay determines PKA in human blood products compliant with the European Pharmacopoeia. The principle of the assay is based on the natural pathway, namely the activation of plasma prekallikrein into kallikrein by the PKA-FXIIa protease. The kallikrein formed releases p-nitroaniline (pNA) from the kallikrein substrate supplied in the assay.

The amount of pNA released is then measured photometrically in a plate reader and is proportional to the amount of PKA present in the blood product up to a concentration of 50 IU/mL. Notably, the assay can be performed as rate method as recommended by the European Pharmacopoeia (EP), or by end point measurement.

[European Pharmacopoeia <0853>, <0255>, <01/2006:0918>; article 114 paragraph 2 of Directive 2001/83/EC; article 1, paragraph 78 of Directive 2004/27/EC]

Environmental Testing

Endocrine disruptors may interfere with the body's endocrine system and produce adverse developmental, reproductive, neurological, and immune effects in humans and wildlife. The presence of vitellogenin in fish is widely used as an indicator of endocrine disruption. TECO offers a new generation of ELISAs for sensitive detection of vitellogenin:

- Applicable to 27 different fish species;
- Testing in mucus, serum and classically in whole body homogenate;
- Non-invasive sampling and repeated testing for drug-induced endocrine disruption;
- Compliant with OECD testing in laboratories;
- Suited for eco-toxicological testing and monitoring.

[German Arzneimittelgesetz (AMG); OECD Guidelines: (229, 230, 234); EC regulation Nr. 440/2008 (REACH, July 2015)]; EU-Guidances 2001/83/EG; 2004/27/EG]

COMING SOON:

Genotoxicity

Drug screening and eco-toxicological assessment requires genotoxicity testing. In accordance with the OECD Guidelines TECO will offer a Mammalian Cell Micronucleus Test (MNvit).

Overview of TECOmedical Products

Biosafety www.tecomedical.com/en/biosafety
Prekallikrein Activator
Liver Toxicology
Kidney Toxicology
Apoptosis
Complement Assays & Reagents - Haemocompatibility

Assays for human and animal application www.tecomedical.com/en/laboratory-ivd-kits-reagents
Diabetes & Obesity
Bone Metabolism
Cartilage Metabolism
Calcium Metabolism
Cardiovascular
Oxidative Stress

Ecotoxicology www.tecomedical.com/en/ecotoxicology
Vitellogenin

www.tecomedical.com

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