


At CXR, we combine our proprietary technologies and world-class scientific expertise to deliver customised preclinical and research solutions. In particular, we offer two key services:

- 1 **Drug Development Solutions** supporting *informed* decision making, avoiding potential problems and accelerating development.
- 2 **Investigative and Mechanistic Toxicology** by understanding the pathways that define the sensitivity of cells to chemicals, we evaluate the *actual* hazard to man of drugs and chemicals.

The Company was established in December 2001 by Professor Roland Wolf & Dr Cliff Elcombe as a spin-out from Dundee University, Scotland and over the past 7 years it has grown into an established profitable business. We have worked with over 60 Pharmaceutical, Biotechnology, Agrochemical, Consumer Product and Chemical companies/consortia of all sizes; including GlaxoSmithKline, AstraZeneca, Schering-Plough, Sanofi-Aventis, Pfizer, Millipore Corporation, TaconicArtemis GmbH, Procter & Gamble, Cancer Research Technology, Ineosfluor, Ineoschlor, Plastics Europe, Dow Agrochemical and ECPI.

The pharmaceutical industry faces an R&D productivity crisis: the cost of bringing an NCE to market (including the cost of failures) was estimated to be around \$320 million in 1991, but had risen to over \$1.2 billion by 2007.

Our goal at CXR is to support informed decision making at all stages of discovery and preclinical drug development, thereby driving lead selection and clinical design decisions that give the highest likelihood of approval with the optimal label. To this end, in addition to offering all standard ADMET screens, we have developed proprietary technologies and services to address key drug development questions: 

Our hits-to-lead programmes combine our proprietary models with improved application of more traditional preclinical techniques and assays, including *in vitro* and *in vivo* ADME and Toxicology studies; cell culture; and an extensive analytical capability (mass spectrometry, HPLC, GC, qPCR, transcription profiling, protein analysis). We also have expertise in traditional biochemical, clinical chemistry and histological techniques.

We work with you in a flexible, consultative and advisory manner to design and interpret programs that deliver the results you need, whilst reducing time, cost and use of animals. Programmes can range from short problem-solving studies, to end-to-end hits-to-lead programmes.

What are the mechanisms of drug action, ADME and toxicity?

Genetically modified *in vivo* and *in vitro* reporter systems rapidly evaluate safety liabilities in animals and cells.

Pre-development *in vivo* screens provide extensive data (PK, drug metabolism, metabolite ID, drug-drug interactions, toxicology, behavioural effects, transcription profiling) to assist in candidate selection prior to regulatory safety studies.

Given this, what confounding factors might impact safety and efficacy?

Proprietary knock-out and transgenic animal models (along with conventional techniques), combined with customised analytics, establish the roles of absorption, drug transport and metabolism on efficacy and toxicity.

What is the relevance of the observed biology to man?

In vitro and *in vivo* model systems more predictive of the human situation (for example humanised murine models) indicate the likely human response to drugs or chemicals.

Clinical trial design optimised through linking preclinical pharmacokinetics and toxicokinetics to efficacy in humans.

Investigative and Mechanistic Toxicology

We elucidate the pathways that define sensitivity of cells to chemicals – modulation of which can result in protective or deleterious effects. We have extensive experience in evaluating toxicological processes across species, and determining the relevance to man of observed adverse reactions to the satisfaction of regulatory bodies. Using this approach, we have ‘rescued’ compounds that may otherwise have been abandoned by industry.

CXR will work with you to design state of the art investigative safety studies to understand the mechanisms of adverse preclinical observations, interpret the results, and if required make recommendations as to the future of the project. Conversely, we can also help you identify chemicals with protective effects.

Advanced applied preclinical and toxicological techniques are used to unravel complex mechanisms of toxicity and to establish their relevance to man. We have expertise in cell culture, *in-vivo* studies, *in vitro* biochemistry and bio-analysis (including laser capture micro-dissection); and combine these with advanced molecular biology, transcription profiling, genomics and bioinformatics, as well as traditional biochemical, clinical chemistry and histological techniques.

CXR also applies and develops new technologies for safety evaluation, and is currently developing panels of transgenic model systems that are more reflective of the human situation, as well as predictive biomarkers of toxicology.

Partnering With CXR

CXR’s collaborative approach, proprietary models and cutting edge technologies have helped numerous ‘blue chip’ companies, as well as smaller organisations, solve issues relating to the the selection of drug candidates or safety of compounds. Our services and partnering models are flexible – we provide services and expertise to perform Drug Development Solutions and Investigative Toxicology on a fee-for-service basis. CXR’s proprietary models are also freely available to licence. We also seek collaborations to develop new models to further improve lead selection and optimisation. For further information on any of our services or technologies, please contact:

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