CardioForesight™

The first comprehensive GLP human cardiovascular safety package.

Biopta Ltd is a Contract Research Organisation specialising in GLP testing in ethically-obtained human tissues. We believe *in vitro* testing in human tissue, the closest model to human *in vivo* function, provides invaluable data to accurately identify compounds with the greatest likelihood of clinical success, reducing the risk of late stage failures and streamlining preclinical development.

The ICH S7A guidelines propose a battery of safety studies which are required to be conducted to GLP standard prior to human exposure. These studies include; cardiovascular assessment, an assessment of central nervous system effects and respiratory function. Routinely, these assessments are carried out in animal *in vivo* models; however at Biopta we are able to provide powerful supporting data in functional human tissues and cells, entirely in compliance with GLP.

Safety profiling in human tissue delivers accurate data on the safety of your compound in man, reducing the extent of *in vivo* animal testing required and eliminating species variation. It is Biopta's recommendation that fully GLP, human *in vitro* safety pharmacology testing is carried out as part of your preclinical development program, delivering powerful human safety data prior to expensive Phase I/IIa studies.

CardioForesight™ comprises:

Human ventricular muscle

Prediction of potential for direct effects on cardiac contractility.

Ventricular muscle and coronary arteries from the same patient can be investigated from healthy hearts sourced from the transplant network.

Human coronary arteries

Prediction of potential for coronary artery vasoconstriction.

Human resistance arteries

Potential to increase or decrease peripheral vascular resistance and hence to alter blood pressure.

hERG assay human cell-based test for IKr blockade

Blockade of IKr potassium channel that plays a key role in ventricular repolarisation and which if blocked is associated with an increased risk of Q-T prolongation and torsades de pointes.

Benefits of Human Tissue Testing

- Strengthens IND submissions
- Avoids species differences
- Adds commercial value by generating human data during preclinical development
- Improves decision-making process based on functional human data
- Reduces the risk of late stage failures

Why use human tissue rather than animal models?

Many animal models represent entirely adequate test systems for specific purposes; however, differences in the typical responses to hormones and neurotransmitters do exist and create uncertainty about the predicted safety profile in humans.

The use of fresh human tissue avoids unforeseen species differences, which can lead to misinterpretation of safety data, not only for drugs that later prove unsafe but also for drugs that may be wrongly classified as unsafe based on responses in animals.

Human coronary arteries

Human coronary arteries contract in response to acetylcholine; in dog coronary arteries there is almost no response to acetylcholine (Ginsburg *et al*.). Similarly, in endothelium intact coronary arteries, 5-HT produces little response in canine arteries, but is a potent vasoconstrictor in human isolated coronary arteries.
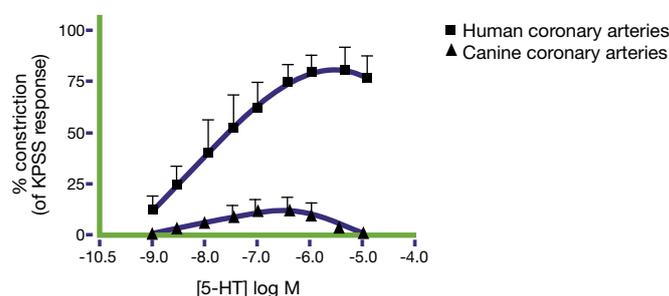
(Biopta observations, see figure 1).

Figure 1. Contractile responses to increasing concentrations of 5-hydroxytryptamine in isolated human (■) and canine (▲) coronary arteries.

References: Ginsburg *et al*. Chest (1980) 78: 180-186