Award

OECD 488 transgenic rodent mutation assay (TGRA) using the Big Blue® rat

UNIVERSITY OF SHEFFIELD

F15: Voluntary ex ante transparency notice
Notice identifier: 2022/S 000-006619
Procurement identifier (OCID): ocds-h6vhtk-032075
Published 10 March 2022, 4:29pm

Section I: Contracting authority/entity

I.1) Name and addresses

UNIVERSITY OF SHEFFIELD

Western Bank

SHEFFIELD

S102TN

Contact

Jamie Shaw

Email

jamie.shaw@sheffield.ac.uk

Country

United Kingdom

NUTS code

UKE32 - Sheffield

Internet address(es)

Main address

https://www.sheffield.ac.uk

I.4) Type of the contracting authority

Body governed by public law

I.5) Main activity

Education

Section II: Object

II.1) Scope of the procurement

II.1.1) Title

OECD 488 transgenic rodent mutation assay (TGRA) using the Big Blue® rat

II.1.2) Main CPV code

- 73111000 - Research laboratory services

II.1.3) Type of contract

Services

II.1.4) Short description

The conduct of an OECD 488 transgenic rodent mutation assay (TGRA) using the Big Blue® rat using cII mutant selection for the University of Sheffield. Studies will be conducted to GLP, and are based on the following preliminary study design:

1. Breeding of target cohort of 40 Big Blue male rats, with delivery to Charles River Laboratories (CRL) facility, Ashland Ohio, USA.

2. Transfer of HPLC analytical method for dose formulation analysis and method transfer summary.

3. Method transfer, validation, homogeneity, solubility and stability work to enable GLP dose formulation analysis during Big Blue® TGRA main study.

4. 7-day dose-range finding study, wild type Fischer F344 male and female rats, to determine limit dose of 1000 mg / kg body weight /day or MTD.

5. Big Blue® TGRA rat main study, male only, using vehicle, 3 dose groups and concurrent positive control. Each group will contain 6 male rats, conducted in accordance with OECD 488; daily test item administration by oral gavage for 28 days (positive control will be dosed days 1, 3, 10, 17 & 24 only); termination and schedule necropsy on day 31 with duodenum and liver removed from all animals, flash frozen and stored prior to shipment to Gentronix Limited.

6. Dose formulation analysis during conduct of the main study.

7. Analysis of liver and duodenum from 5 animals per dose group in the in vitro phase of

the Big Blue® TGRA study as per OECD 488 will be conducted at Gentronix Limited. DNA will be extracted, packaged into lambda bacteriophage used to infect E. coli strain G1250 to determine phage packaging efficiency and cII mutation detection after plating on agar. Phage packaging titres of at least 125,000 per animal will be determined, to facilitate estimation of mutation frequency.

8. GLP reporting of results.

II.1.6) Information about lots

This contract is divided into lots: No

II.1.7) Total value of the procurement (excluding VAT)

Lowest offer: £320,000 / Highest offer: £350,000 taken into consideration

II.2) Description

II.2.3) Place of performance

NUTS codes

- UKD62 - Cheshire East

Main site or place of performance

The majority of the work will be performed in Alderley Edge, Cheshire with c33% of the work (in-life) sub-contracted to Charles River Laboratories in Ohio, USA

II.2.4) Description of the procurement

In August 2021 the University of Sheffield entered into a contract with Wuxi AppTec (Hong Kong) Ltd (Find A Tender Service Contract Award Notice Publication Reference: 2021/S 000-021618) for the provision of IND enabling toxicology study services for M102 (small-molecule drug candidate; oral route, once daily), including 2 animal studies.

It is now the intention of the University of Sheffield to contract the third animal study (Big Blue) to Gentronix Limited. Studies will be conducted to GLP, and are based on the following preliminary study design:

1. Breeding of target cohort of 40 Big Blue male rats, with delivery to CRL facility, Ashland Ohio.

2. Transfer of HPLC analytical method for dose formulation analysis and method transfer summary.

3. Method transfer, validation, homogeneity, solubility and stability work to enable GLP dose formulation analysis during Big Blue® TGRA main study.

4. 7-day dose-range finding study, wild type Fischer F344 male and female rats, to determine limit dose of 1000 mg / kg body weight /day or MTD.

5. Big Blue® TGRA rat main study, male only, using vehicle, 3 dose groups and concurrent positive control. Each group will contain 6 male rats, conducted in accordance with OECD 488; daily test item administration by oral gavage for 28 days (positive control will be dosed days 1, 3, 10, 17 & 24 only); termination and schedule necropsy on day 31 with duodenum and liver removed from all animals, flash frozen and stored prior to shipment to Gentronix Limited.

6. Dose formulation analysis during conduct of the main study.

7. Analysis of liver and duodenum from 5 animals per dose group in the in vitro phase of the Big Blue® TGRA study as per OECD 488 will be conducted at Gentronix Limited. DNA will be extracted, packaged into lambda bacteriophage used to infect E. coli strain G1250 to determine phage packaging efficiency and cII mutation detection after plating on agar. Phage packaging titres of at least 125,000 per animal will be determined, to facilitate estimation of mutation frequency.

8. GLP reporting of results.

The preliminary study design does not include any bioanalytical analysis for toxicokinetic or proof-of-exposure endpoints in e.g. rat plasma. This may be required at a later date and the cost is included in the cost range provided.

Schedule - subject to CRL timelines and Study Plan

• In-life study phases commence at CRL - Dec 2022

• In-life study phases complete at CRL - Jan 2022

• Post-life in vitro phases commence at Gentronix Limited - Feb 2022

• Post-life in vitro phases complete at Gentronix Limited - April 2023

• Draft report - by end May 2023

The CRL outsourced portion is currently estimated to be ~£110k of the c£320k. The remainder relates to Animal breeding or activities undertaken by Gentronix Limited.

Gentronix's Limited's choice of partnership with CRL was based on 4 main factors:

1. They are a significant contract research organisation, high animal welfare standards and with capabilities at their Ashland facilities to conduct all necessary aspects of the in-life Big Blue studies. These include supporting toxicological and analytical endpoints and in particular they have coverage for all expected routes of exposure/administration including via inhalation.

2. The laboratory team at Ashland has previous experience of acting as GLP main test site and Study Director for Big Blue® studies, commissioned by the previous asset owner being BioReliance Corporation. This substantially de-risks the GLP compliance elements of these studies, and was viewed favourably in our discussions with the UK MHRA prior to commencing work on this project.

3. The USA location and relative close proximity to our animal facility breeding location in NY. This enables ground transportation of animals within a timeframe that provides no compromise on animal welfare and shipments are routine from our contract breeder to these facilities.

4. In many circumstances they were and are an established service provider to the same clients Gentronix Limited receives enquiries from for Big Blue® studies. This de-risks commercial, contractual and legal discussions.

At present the CRL Ashland facility is the only site capable of conducting GLP compliant in-life subcontract work for Big Blue studies on behalf of Gentronix Limited.

II.2.5) Award criteria

Price

II.2.11) Information about options

Options: No

II.2.14) Additional information

This contract is exempt under Regulation 14 of PCR 2015.

However in the interests of transparency, in addition to applying Regulation 14 then Regulation 32 of PCR 2015 is being applied as in 32. (2) (b) (ii).

No contract will be entered into until after a 10 day calendar day period from the submission of the VEAT notice date.

Section IV. Procedure

IV.1) Description

IV.1.1) Type of procedure

Negotiated without a prior call for competition

- The works, supplies or services can be provided only by a particular economic operator for the following reason:
    - absence of competition for technical reasons

Explanation:

BigBlue test and MutaMouse test are both qualified genotoxicity studies using transgenic rodent models to enable the US FDA investigational new drug (IND) filing and the initiation of first-in-human studies. BigBlue assay uses transgenic rats, while MutaMouse assay uses transgenic mice.

To identify the rodent and non-rodent species relevant to human, the research teams at UoS and its partners (including Aclipse) have conducted a metabolite identification study. Potential metabolites of M102 were identified and possible metabolic pathways were predicted in liver microsomes from various species (mouse, rat, dog, monkey, human). It was observed that the metabolites in human liver microsomes were relevant to those of rats and monkey. As a result, rat and monkey were selected as appropriate rodent and non-rodent species for toxicological evaluations for M102. In fact, the non-GLP M102 general toxicological study in rats has already been performed which makes the BigBlue assay the next scientifically logical step. The use of BigBlue assay (i.e., transgenic rat model) to evaluate the in vivo genotoxicity of M102 can be well justified.

Gentronix (Limited have proprietary ownership of the Big Blue genetically specific breeding colony and methodology, meaning that there are no other CLP compliant providers who can provide this assay.

A single source is therefore proposed to formalise the solution provided by Gentronix Limited for the reasons that it has proprietary ownership of the Big Blue® Transgenic Rodent (TGR) Gene Mutation Assay which is stipulated in order to obtain FDA approval.

The Services to be delivered will commence around December 2022, are due to take 6 months and complete by May 2023.

IV.1.8) Information about the Government Procurement Agreement (GPA)

The procurement is covered by the Government Procurement Agreement: Yes

Section V. Award of contract/concession

A contract/lot is awarded: Yes

V.2) Award of contract/concession

V.2.1) Date of conclusion of the contract

10 March 2022

V.2.2) Information about tenders

The contract has been awarded to a group of economic operators: No

V.2.3) Name and address of the contractor/concessionaire

Gentronix Limited

Cheshire

Country

United Kingdom

NUTS code

- UKD62 - Cheshire East

The contractor/concessionaire is an SME

No

V.2.4) Information on value of contract/lot/concession (excluding VAT)

Initial estimated total value of the contract/lot/concession: £320,000

Lowest offer: £320,000 / Highest offer: £350,000 taken into consideration

V.2.5) Information about subcontracting

The contract/lot/concession is likely to be subcontracted

Value or proportion likely to be subcontracted to third parties

Value excluding VAT: £110,000

Short description of the part of the contract to be subcontracted

the in-life studies will be sub-contracted

Section VI. Complementary information

VI.4) Procedures for review

VI.4.1) Review body

High Court of England, Wales & Northern Ireland

London

Country

United Kingdom