When is CoU discussed?
How is it done?
Who is involved?
What is discussed?
Where do we capture it?

R. Hughes, Resolian

When is CoU discussed?

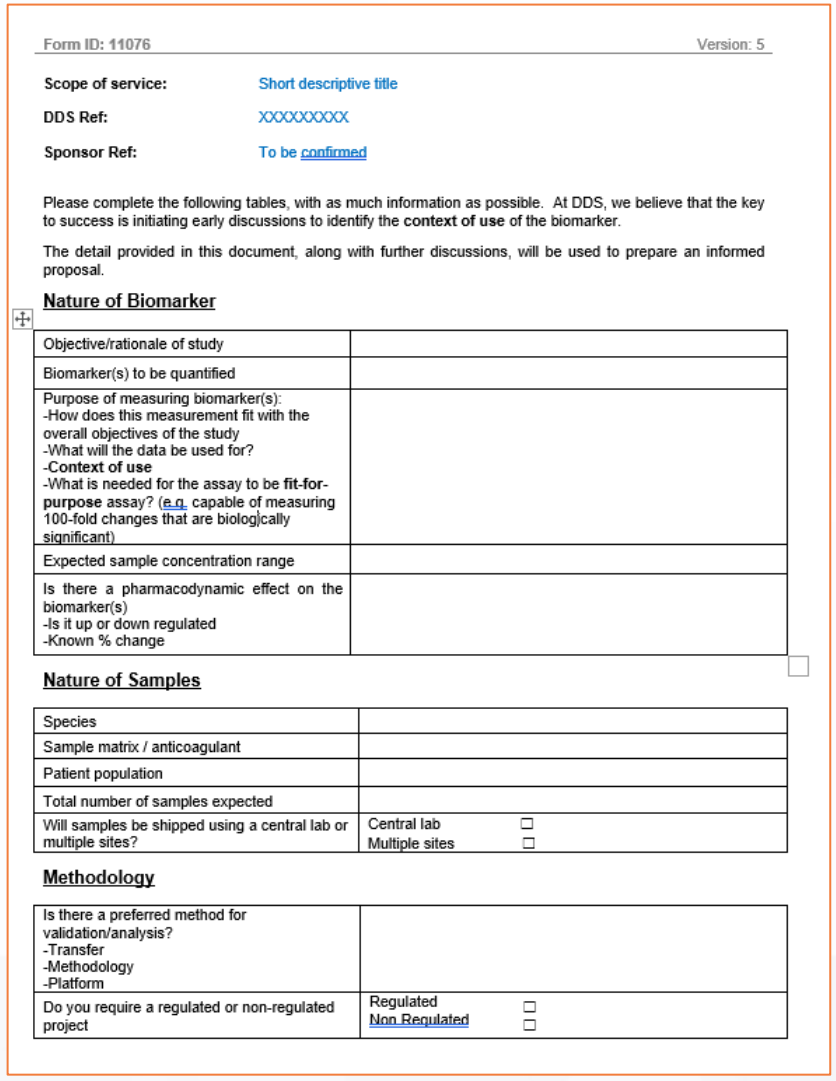
RESOLIAN

- All biomarker enquiries* → Biomarker Request Questionnaire

* New enquiries, follow on sample analysis, or new sample analysis using a previously characterised method

How is it done?

RESOLIAN



Form ID: 11076 Version: 5

Scope of service: Short descriptive title

DDS Ref: XXXXXXXXX

Sponsor Ref: To be confirmed

Please complete the following tables, with as much information as possible. At DDS, we believe that the key to success is initiating early discussions to identify the **context of use** of the biomarker.

The detail provided in this document, along with further discussions, will be used to prepare an informed proposal.

Nature of Biomarker

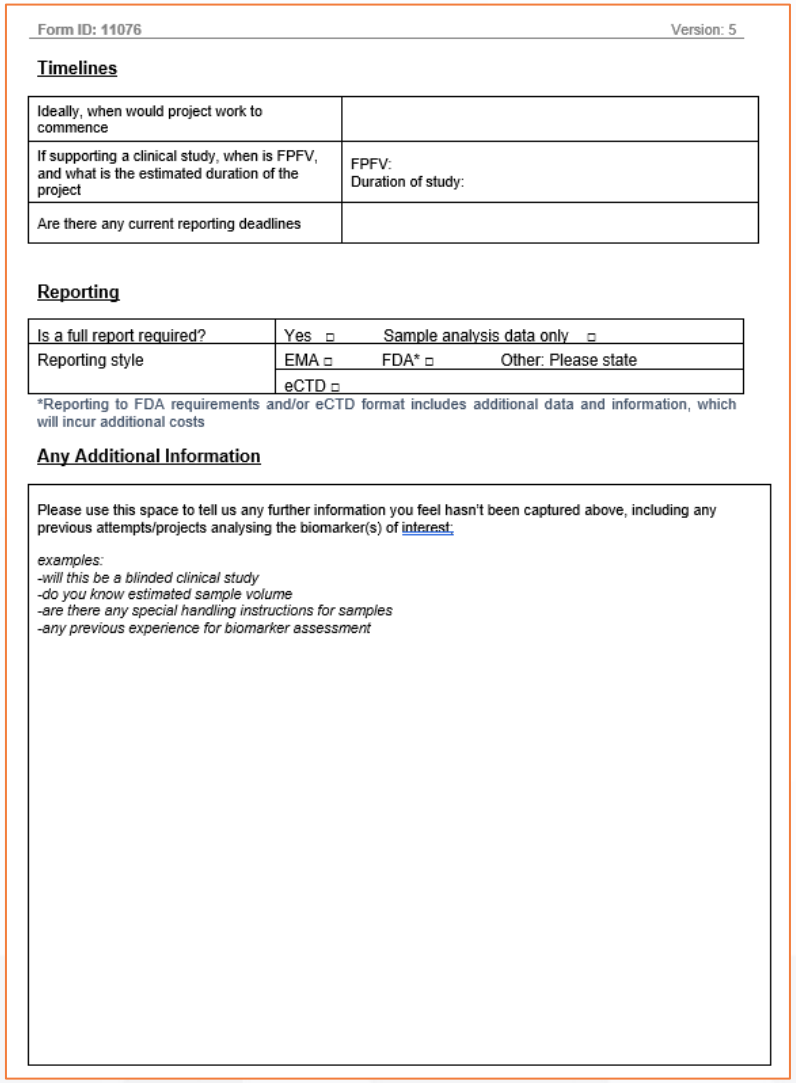
Objective/rationale of study	
Biomarker(s) to be quantified	
Purpose of measuring biomarker(s): -How does this measurement fit with the overall objectives of the study -What will the data be used for? -**Context of use** -What is needed for the assay to be **fit-for-purpose** assay? (e.g. capable of measuring 100-fold changes that are biologically significant)	
Expected sample concentration range	
Is there a pharmacodynamic effect on the biomarker(s) -Is it up or down regulated -Known % change	

Nature of Samples

Species	
Sample matrix / anticoagulant	
Patient population	
Total number of samples expected	
Will samples be shipped using a central lab or multiple sites?	Central lab ☐ Multiple sites ☐

Methodology

Is there a preferred method for validation/analysis? -Transfer -Methodology -Platform	
Do you require a regulated or non-regulated project	Regulated ☐ Non Regulated ☐



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Timelines

Ideally, when would project work to commence	
If supporting a clinical study, when is FPFV, and what is the estimated duration of the project	FPFV: Duration of study:
Are there any current reporting deadlines	

Reporting

Is a full report required?	Yes ☐	Sample analysis data only ☐
Reporting style	EMA ☐ FDA* ☐	Other: Please state
	eCTD ☐	

*Reporting to FDA requirements and/or eCTD format includes additional data and information, which will incur additional costs

Any Additional Information

Please use this space to tell us any further information you feel hasn't been captured above, including any previous attempts/projects analysing the biomarker(s) of interest:

examples:
-will this be a blinded clinical study
-do you know estimated sample volume
-are there any special handling instructions for samples
-any previous experience for biomarker assessment

Questionnaire

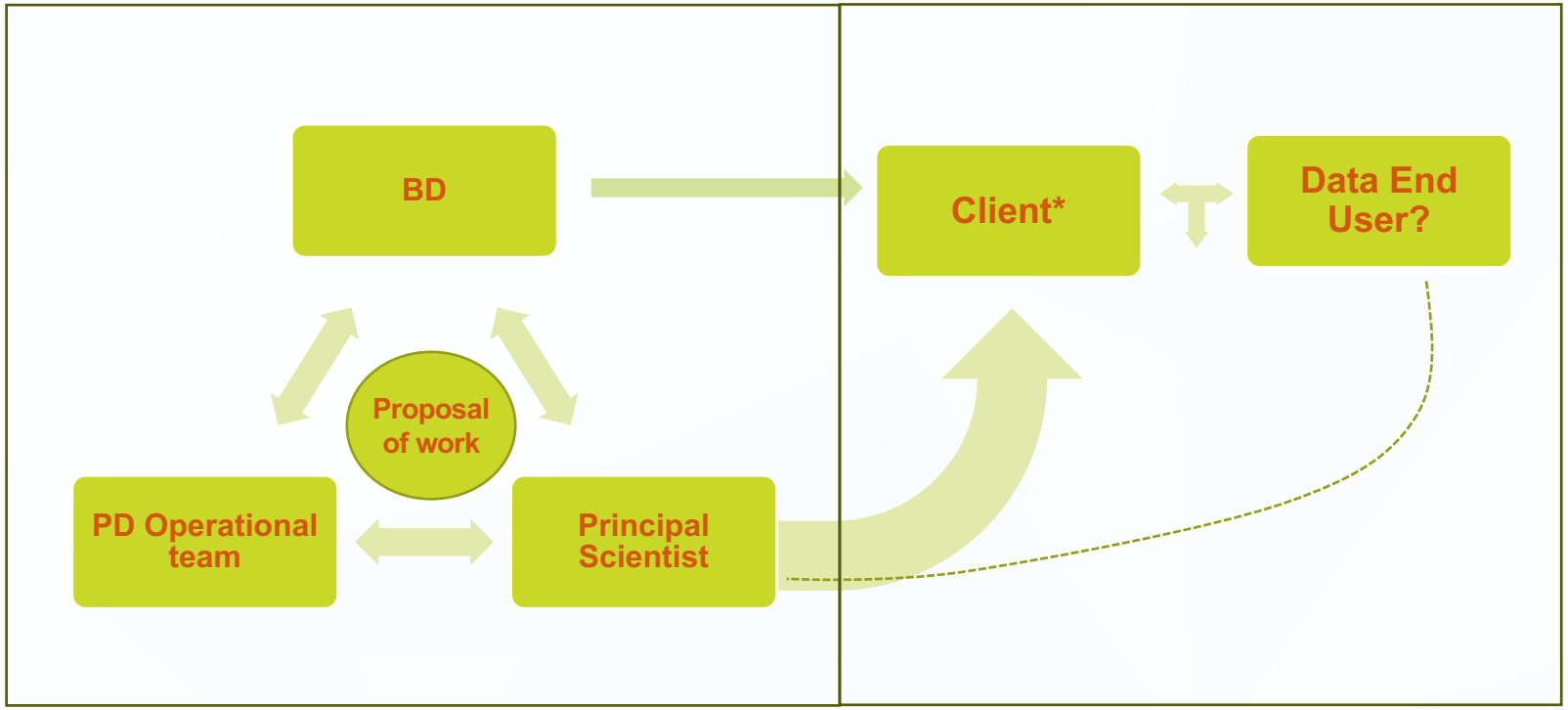
Provided by BD via email to Sponsor representative

Free text

Ultimately gets saved on company network in a BD location alongside the proposal

Who is involved?

RESOLIAN



*Client could be
Central lab
Clinical trial unit
3rd party Consultant
Outsourcing manager
Translational lead
BioA lab

What is discussed?

RESOLIAN

Nature of Biomarker
Objective/rationale of study
Biomarker(s) to be quantified
Purpose of measuring biomarker(s):
How does this measurement fit with the overall objectives of the study
What will the data be used for?
Context of use
-What is needed for the assay to be fit-for-purpose assay? (e.g. capable of measuring 100-fold changes that are biologically significant)
Expected sample concentration range
Is there a pharmacodynamic effect on the biomarker(s)
-Is it up or down regulated
-Known % change

Methodology
Samples (no., population, matrix, how they will arrive)
Timelines
Reporting requirements
AOB

Objective/rationale of study	Understand mechanism of action of our drug
Biomarker(s) to be quantified	[redacted]2
Purpose of measuring biomarker(s): -How does this measurement fit with the overall objectives of the study -What will the data be used for? -**Context of use** -What is needed for the assay to be **fit-for-purpose** assay? (e.g. capable of measuring 100-fold changes that are biologically significant)	[redacted]2 is a downstream target of IL[redacted] signalling. The data will be used to understand the mechanism of action of the drug. Plasma samples from healthy individuals will be used for this analysis
Expected sample concentration range	10-300 pg/ml
Is there a pharmacodynamic effect on the biomarker(s) -Is it up or down regulated -Known % change	Down regulated

What is discussed?

RESOLIAN

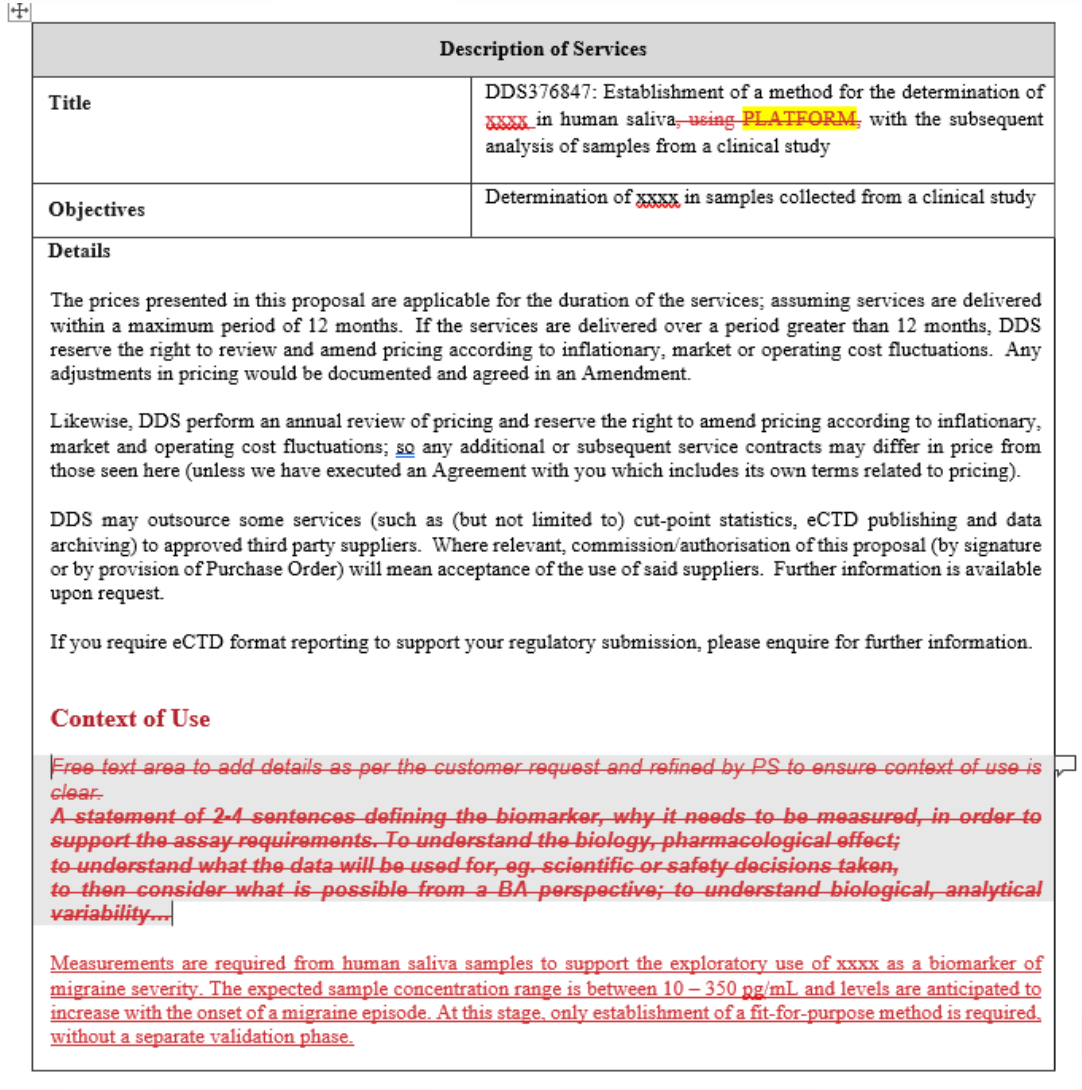
Nature of Biomarker
Objective/rationale of study
Biomarker(s) to be quantified
Purpose of measuring biomarker(s):
How does this measurement fit with the overall objectives of the study
What will the data be used for?
Context of use
-What is needed for the assay to be fit-for-purpose assay? (e.g. capable of measuring 100-fold changes that are biologically significant)
Expected sample concentration range
Is there a pharmacodynamic effect on the biomarker(s)
-Is it up or down regulated
-Known % change

Methodology
Samples (no., population, matrix, how they will arrive)
Timelines
Reporting requirements
AOB

Objective/rationale of study	This Ph1 study aims to characterise the safety and tolerability (primary endpoint) and pharmacology (secondary and exploratory) of [redacted], a bispecific monoclonal antibody to [redacted] and [redacted]
Biomarker(s) to be quantified	[redacted] enzyme activity on [redacted] (output: relative activity units with recombinant [redacted] as a standard)
Purpose of measuring biomarker(s): -How does this measurement fit with the overall objectives of the study -What will the data be used for? -**Context of use** -What is needed for the assay to be **fit-for-purpose** assay? (e.g. capable of measuring 100-fold changes that are biologically significant)	The [redacted] activity assay will be an exploratory endpoint for the Ph1 trial, but data will be used internally as part of our PK/PD dose modelling and has been built into our internal go/no go decision framework for the study. Data will be used as % total activity (total activity being an individual's baseline activity), however [redacted] in house development suggests a target assay range of 0.78-400 ng/mL [redacted] equivalent activity units is sufficient to measure baseline activity in healthy volunteers and RA patients with 90% inhibition from baseline being the go/no go target for the Ph1 study. Robustness and reproducibility ~EC80 and ~EC5 of the assay must be within 15% CV
Expected sample concentration range	1.5-200 activity units
Is there a pharmacodynamic effect on the biomarker(s) -Is it up or down regulated -Known % change	Yes, marker will decrease with increasing drug exposure. Expected inhibition is 90% at later dose levels in the SAD.

Where do we capture it?

- Proposal stage
  - This will involve a member of the Principal Scientist team interpreting and translating the information from the questionnaire into a SoW which outlines how we plan to support these requirements
  - No CoU = Assay characterisation
  - + CoU = FFP validation
  - Becomes difficult with Sponsor-specific WO
- Analytical Plan



Description of Services	
Title	DDS376847: Establishment of a method for the determination of ~~xxxx~~ in human saliva~~, using PLATFORM,~~ with the subsequent analysis of samples from a clinical study
Objectives	Determination of ~~xxxx~~ in samples collected from a clinical study

Details

The prices presented in this proposal are applicable for the duration of the services; assuming services are delivered within a maximum period of 12 months. If the services are delivered over a period greater than 12 months, DDS reserve the right to review and amend pricing according to inflationary, market or operating cost fluctuations. Any adjustments in pricing would be documented and agreed in an Amendment.

Likewise, DDS perform an annual review of pricing and reserve the right to amend pricing according to inflationary, market and operating cost fluctuations; so any additional or subsequent service contracts may differ in price from those seen here (unless we have executed an Agreement with you which includes its own terms related to pricing).

DDS may outsource some services (such as (but not limited to) cut-point statistics, eCTD publishing and data archiving) to approved third party suppliers. Where relevant, commission/authorisation of this proposal (by signature or by provision of Purchase Order) will mean acceptance of the use of said suppliers. Further information is available upon request.

If you require eCTD format reporting to support your regulatory submission, please enquire for further information.

Context of Use

~~*Free text area to add details as per the customer request and refined by PS to ensure context of use is clear.*~~
~~***A statement of 2-4 sentences defining the biomarker, why it needs to be measured, in order to support the assay requirements. To understand the biology, pharmacological effect;***~~
~~***to understand what the data will be used for, eg. scientific or safety decisions taken,***~~
~~***to then consider what is possible from a BA perspective; to understand biological, analytical variability…***~~

Measurements are required from human saliva samples to support the exploratory use of xxxx as a biomarker of migraine severity. The expected sample concentration range is between 10 – 350 pg/mL and levels are anticipated to increase with the onset of a migraine episode. At this stage, only establishment of a fit-for-purpose method is required, without a separate validation phase.

Where do we capture it?

- Proposal stage
- Analytical Plan
  - Project life cycle
- Report?

5 Introduction

5.1 Analytical project objectives

The purpose of this analytical project is to characterise a colorimetric ELISA method for the measurement of renin in human plasma over the calibration range 2000 – 31.3 pg/mL.

The analytical method is intended for use as a fit for purpose method for the measurement of renin in human plasma samples. As the context of use is not explicitly defined, this project will aim to characterise the analytical performance of the assay to enable the Sponsor to assess its suitability to support their clinical endpoints.

5 Introduction

5.1 Study objectives

The purpose of this study is to validate a CSF method for the measurement of bound [redacted] in cynomolgus monkey CSF over the calibration range 0.956 – 1000 pg/mL. The method to be validated was developed in study LGC353517QB01.

Pre-validation assessments, performed under the development study, included labelling and establishment of capture and detection reagents, optimisation, QC preparation and assessment of intra and inter-assay precision. Following completion of the development a pre-validation data was reviewed by DDS principal scientists and was deemed suitable to support the context of use and for progression to validation.

The context of use of the method is to determine fold-level changes in bound [redacted] concentrations following dosing of [redacted] (a surrogate molecule for clinical compound [redacted]). Baseline samples will only consist of the unbound fraction of [redacted] and will therefore be BLQ. Following dosing of [redacted], an increase is expected in bound [redacted] concentrations over-time, with later timepoints expected to be around ULOQ. Data generated from subsequent sample analysis studies will be analysed in combination with data from the total CSF [redacted] method and will be used to evaluate drug target binding and thus will support critical pharmacodynamic endpoints for use as part of a regulatory submission. As such, this validation will follow a category 1 (Tier 2) validation structure, as detailed in "Validation – Ligand Binding Assays for Biomarkers" (Qualtrax ID: 5338) and this study plan, to ensure the method is fit for purpose to support the context of use.