Health Canada and the Public Health Agency of Canada | Santé Canada et l'Agence de la santé publique du Canada

RETURN BIDS TO:
RETOURNER LES SOUMISSIONS À:

Health Canada / Santé Canada

Attn: Cathy Jones
Email: *cathy.jones@canada.ca*

REQUEST FOR PROPOSAL
DEMANDE DE PROPOSITION

Proposal To: Health Canada
We hereby offer to sell to Her Majesty the Queen in right of Canada, in accordance with the terms and conditions set out herein, referred to herein or attached hereto, the goods, services, and construction listed herein and on any attached sheets at the price(s) set out thereof.

Proposition à:
Santé Canada
Nous offrons par la présente de vendre à Sa Majesté la Reine du chef du Canada, aux conditions énoncées ou incluses par référence dans la présente et aux annexes ci-jointes, les biens, services et construction énumérés ici sur toute feuille ci-annexées, au(x) prix indiqué(s).

Instructions : See Herein
Instructions: Voir aux présentes

Issuing Office – Bureau de distribution
Health Canada / Santé Canada
200, Eglantine Driveway
Tunney's Pasture
Ottawa Ontario K1A 0K9

Title – Sujet **Mu Opioid Receptor (MOR) activity profile testing for fentanyl analogues.**	
Solicitation No. – N° de l'invitation 1000222004	**Date** July 10, 2020
Solicitation Closes at – 2 :00PM **L'invitation prend fin à** **on / le – August 4th, 2020**	**Time Zone** **Fuseau horaire** EST 2 :00pm
F.O.B. - F.A.B. **Plant-Usine:** ☐ **Destination:** ☒ **Other-Autre:** ☐	
Address Enquiries to: - Adresser toutes questions à : Name: Cathy Jones Email: cathy.jones@canada.ca Telephone – téléphone : 613-298-8295	
Destination – of Goods, Services, and Construction: **Destination – des biens, services et construction :** See Herein – Voir ici	
Delivery required - Livraison exigée See Herein – Voir ici	
Vendor/firm Name and address **Raison sociale et adresse du fournisseur/de l'entrepreneur** **TBA** **Facsimile No. – N° de télécopieur :** **Telephone No. – N° de téléphone :**	
Name and title of person authorized to sign on behalf of Vendor/firm **Nom et titre de la personne autorisée à signer au nom du fournisseur/de l'entrepreneur** _____ **(type or print)/ (taper ou écrire en caractères d'imprimerie)** _____ _____ **Signature** **Date**	

Canada

TABLE OF CONTENTS

PART 1 - GENERAL INFORMATION 3

1.1 SECURITY REQUIREMENTS 3
1.2 STATEMENT OF WORK 3
1.3 DEBRIEFINGS 3

PART 2 - BIDDER INSTRUCTIONS 4

2.1 STANDARD INSTRUCTIONS, CLAUSES AND CONDITIONS 4
2.2 SUBMISSION OF BIDS 4
2.3 FORMER PUBLIC SERVANT 5
2.4 ENQUIRIES - BID SOLICITATION 6
2.5 APPLICABLE LAWS 6

PART 3 - BID PREPARATION INSTRUCTIONS 7

3.1 BID PREPARATION INSTRUCTIONS 7

PART 4 - EVALUATION PROCEDURES AND BASIS OF SELECTION 9

4.1 EVALUATION PROCEDURES 9
4.2 BASIS OF SELECTION 15

PART 5 – CERTIFICATIONS AND ADDITIONAL INFORMATION 17

5.1 CERTIFICATIONS REQUIRED WITH THE BID 17
5.2 CERTIFICATIONS PRECEDENT TO CONTRACT AWARD AND ADDITIONAL INFORMATION 17

PART 6 - RESULTING CONTRACT CLAUSES 19

6.1 SECURITY REQUIREMENTS 19
6.2 STATEMENT OF WORK *OR* REQUIREMENT 19
6.3 STANDARD CLAUSES AND CONDITIONS 19
6.4 TERM OF CONTRACT 19
6.5 AUTHORITIES 19
6.6 PROACTIVE DISCLOSURE OF CONTRACTS WITH FORMER PUBLIC SERVANTS 20
6.7 PAYMENT 20
6.8 INVOICING INSTRUCTIONS 23
6.9 CERTIFICATIONS AND ADDITIONAL INFORMATION 23
6.10 APPLICABLE LAWS 23
6.11 PRIORITY OF DOCUMENTS 23

ANNEX "A" 24

STATEMENT OF WORK 24

ANNEX "B" 33

SECURITY REQUIREMENTS CHECK LIST 33

ANNEX “C” TO PART 3 OF THE BID SOLICITATION 34

ELECTRONIC PAYMENT INSTRUMENTS 34

PART 1 - GENERAL INFORMATION

The bid solicitation is divided into seven parts plus attachments and annexes, as follows:

Part 1 General Information: provides a general description of the requirement;

Part 2 Bidder Instructions: provides the instructions, clauses and conditions applicable to the bid solicitation;

Part 3 Bid Preparation Instructions: provides Bidders with instructions on how to prepare their bid;

Part 4 Evaluation Procedures and Basis of Selection: indicates how the evaluation will be conducted, the evaluation criteria that must be addressed in the bid, and the basis of selection;

Part 5 Certifications and Additional Information: includes the certifications and additional information to be provided;

Part 6 Security, Financial and Other Requirements: includes specific requirements that must be addressed by Bidders; and

Part 7 Resulting Contract Clauses: includes the clauses and conditions that will apply to any resulting contract.

1.1 Security Requirements

There are no Security Requirements associated with this RFP

1.2 Statement of Work

Health Canada requires the services of a Contractor to conduct *MU Opioid Receptor (MOR) activity profile testing for fentanyl analogues.* A minimum of one (1) Project Manager and one (1) Laboratory Technician are required.

The Work to be performed is detailed under Annex A

1.3 Debriefings

Bidders may request a debriefing on the results of the bid solicitation process. Bidders should make the request to the Contracting Authority within 15 working days from receipt of the results of the bid solicitation process. The debriefing may be in writing, by telephone or in person.

PART 2 - BIDDER INSTRUCTIONS

2.1 Standard Instructions, Clauses and Conditions

All instructions, clauses and conditions identified in the bid solicitation by number, date and title are set out in the Standard Acquisition Clauses and Conditions Manual (https://buyandsell.gc.ca/policy-and-guidelines/standard-acquisition-clauses-and-conditions-manual) issued by Public Works and Government Services Canada.

Bidders who submit a bid agree to be bound by the instructions, clauses and conditions of the bid solicitation and accept the clauses and conditions of the resulting contract.

The 2003 Standard Instructions - Goods or Services - Competitive Requirements, are incorporated by reference into and form part of the bid solicitation.

"Subsections 04 and 05 of Section 01 Integrity Provisions - Bid of the Standard Instructions *(2003)* incorporated by reference above are deleted in their entirety and replaced with the following:

4. Bidders who are incorporated or who are a sole proprietorship, including those bidding as a joint venture, have already provided a list of names of all individuals who are directors of the Bidder, or the name of the owner, at the time of submitting an arrangement under the Request for Supply Arrangement (RFSA). These bidders must diligently inform Canada in writing of any changes affecting the list of directors during this procurement process as well as during the contract period.
5. Canada may, at any time, request that a bidder provide properly completed and Signed Consent Forms (Consent to a Criminal Record Verification form - PWGSC-TPSGC 229) for any or all individuals mentioned above within a specified time frame. Failure to provide such consent forms and associated information within the time frame provided, or failure to cooperate to the verification process, will result in the bid being declared non-responsive."

Subsection 5.4 of 2003, Standard Instructions - Goods or Services - Competitive Requirements, is amended as follows:

Delete: 60 days
Insert: 180 days

2.2 Submission of Bids

Bids must be submitted only to the contracting officer, Cathy Jones by the date, time and place indicated on page 1 of the bid solicitation.

You are invited to submit electronic copies in either official language (English or French) of both the Technical and Cost Proposals. The RFP Reference Number and the title of the Requirement must be in the subject line of your email and your proposal must be structured in accordance to section 3.1.

No price or cost information should appear in any other section of the bid. Failure to provide the Financial Bid in a separate attachment will render a bid non-responsive.

If the email including attachments is larger than 20mb, please submit your bid in separate emails to not exceed Health Canada's server limitation.

2.2.1 Bidders who submit a bid in response to this RFP agree to be bound by the instructions, clauses and conditions of the RFP and accept the terms and conditions of the resulting contract.

2.2.2 It is the Bidder's responsibility to obtain, if necessary, clarification of the requirements contained in the RFP and to prepare its bid in accordance with the instructions contained in the RFP. Enquiries must be submitted in writing to the Contracting Authority identified in Part 6, Section 6.5.1 and in accordance with section 2.4 (Enquiries).

2.2.3 The RFP documents contain all the requirements relating to the bid solicitation. Any other information or documentation provided to or obtained by a Bidder from any other source is not relevant and not part of this RFP. Bidders should not assume that practices used under previous RFPs or contracts will continue, unless they are identified in the RFP. Bidders should also not assume that their existing capabilities meet the requirements of the RFP simply because they have met previous requirements.

2.3 Former Public Servant

Contracts awarded to former public servants (FPS) in receipt of a pension or of a lump sum payment must bear the closest public scrutiny, and reflect fairness in the spending of public funds. In order to comply with Treasury Board policies and directives on contracts awarded to FPSs, bidders must provide the information required below before contract award. If the answer to the questions and, as applicable the information required have not been received by the time the evaluation of bids is completed, Canada will inform the Bidder of a time frame within which to provide the information. Failure to comply with Canada's request and meet the requirement within the prescribed time frame will render the bid non-responsive.

Definitions

For the purposes of this clause,"former public servant" is any former member of a department as defined in the *Financial Administration Act*, R.S., 1985, c. F-11, a former member of the Canadian Armed Forces or a former member of the Royal Canadian Mounted Police. A former public servant may be:

a. an individual;

b. an individual who has incorporated;

c. a partnership made of former public servants; or

d. a sole proprietorship or entity where the affected individual has a controlling or major interest in the entity.

"lump sum payment period" means the period measured in weeks of salary, for which payment has been made to facilitate the transition to retirement or to other employment as a result of the implementation of various programs to reduce the size of the Public Service. The lump sum payment period does not include the period of severance pay, which is measured in a like manner.

"pension" means a pension or annual allowance paid under the *Public Service Superannuation Act* (PSSA), R.S., 1985, c. P-36, and any increases paid pursuant to the *Supplementary Retirement Benefits Act*, R.S., 1985, c. S-24 as it affects the PSSA. It does not include pensions payable pursuant to the *Canadian Forces Superannuation Act*, R.S., 1985, c. C-17, the *Defence Services Pension Continuation Act*, 1970, c. D-3, the *Royal Canadian Mounted Police Pension Continuation Act* , 1970, c. R-10, and the *Royal Canadian Mounted Police Superannuation Act*, R.S., 1985, c. R-11, the *Members of Parliament Retiring Allowances Act*, R.S. 1985, c. M-5, and that portion of pension payable to the *Canada Pension Plan Act*, R.S., 1985, c. C-8.

Former Public Servant in Receipt of a Pension

As per the above definitions, is the Bidder a FPS in receipt of a pension? **Yes** ( ) **No** ( )

If so, the Bidder must provide the following information, for all FPSs in receipt of a pension, as applicable:

a. name of former public servant;

b. date of termination of employment or retirement from the Public Service.

By providing this information, Bidders agree that the successful Bidder's status, with respect to being a former public servant in receipt of a pension, will be reported on departmental websites as part of the published proactive disclosure reports in accordance with Contracting Policy Notice: 2012-2 and the Guidelines on the Proactive Disclosure of Contracts.

Work Force Adjustment Directive

Is the Bidder a FPS who received a lump sum payment pursuant to the terms of the Work Force Adjustment Directive? **Yes** ( ) **No** ( )

If so, the Bidder must provide the following information:

a. name of former public servant;

b. conditions of the lump sum payment incentive;

c. date of termination of employment;

d. amount of lump sum payment;

e. rate of pay on which lump sum payment is based;

f. period of lump sum payment including start date, end date and number of weeks;

g. number and amount (professional fees) of other contracts subject to the restrictions of a work force adjustment program.

For all contracts awarded during the lump sum payment period, the total amount of fees that may be paid to a FPS who received a lump sum payment is $5,000, including Applicable Taxes.

2.4 Enquiries - Bid Solicitation

All enquiries must be submitted in writing to the Contracting Authority no later than five (5) calendar days before the bid closing date. Enquiries received after that time may not be answered.

Bidders should reference as accurately as possible the numbered item of the bid solicitation to which the enquiry relates. Care should be taken by Bidders to explain each question in sufficient detail in order to enable Canada to provide an accurate answer. Technical enquiries that are of a proprietary nature must be clearly marked "proprietary" at each relevant item. Items identified as "proprietary" will be treated as such except where Canada determines that the enquiry is not of a proprietary nature. Canada may edit the question(s) or may request that the Bidder do so, so that the proprietary nature of the question(s) is eliminated and the enquiry can be answered to all Bidders. Enquiries not submitted in a form that can be distributed to all Bidders may not be answered by Canada.

2.5 Applicable Laws

Any resulting contract must be interpreted and governed, and the relations between the parties determined, by the laws in force in Ontario.

Bidders may, at their discretion, substitute the applicable laws of a Canadian province or territory of their choice without affecting the validity of their bid, by deleting the name of the Canadian province or territory specified and inserting the name of the Canadian province or territory of their choice. If no change is made, it acknowledges that the applicable laws specified are acceptable to the Bidders.

PART 3 - BID PREPARATION INSTRUCTIONS

3.1 Bid Preparation Instructions

The bid must be gathered per section and separated as follows:

Canada requests that Bidders provide their offer in separate sections as follows (Bidders choose A or B as their submission method):

A. For electronic bid submissions via e-mail:

Section I: Technical Bid (one (1) electronic copy submitted via e-mail)
Section II: Financial Bid (one (1) electronic copy submitted via e-mail)
Section III: Certifications (one (1) electronic copy submitted via e-mail)

B. For hard-copy submissions to Bid Receiving Unit:

Section I: Technical Bid (four (4) hard-copies and one (1) soft copy via CD)
Section II: Financial Bid (one (1) hard-copy and one (1) soft copy via CD)
Section III: Certifications (one (1) hard-copy and one (1) soft copy via CD)

If there is a discrepancy between the wording of the soft copy and the hard copy, the wording of the hard copy will have priority over the wording of the soft copy.

Prices must appear in the financial offer only. No prices must be indicated in any other section of the offer.

Canada requests that bidders follow the format instructions described below in the preparation of hard copy of their bid:

(a) use 8.5 x 11 inch (216 mm x 279 mm) paper;
(b) use a numbering system that corresponds to the bid solicitation.

In April 2006, Canada issued a policy directing federal departments and agencies to take the necessary steps to incorporate environmental considerations into the procurement process Policy on Green Procurement (https://www.tbs-sct.gc.ca/pol/doc-eng.aspx?id=32573). To assist Canada in reaching its objectives, bidders should:

1) use 8.5 x 11 inch (216 mm x 279 mm) paper containing fibre certified as originating from a sustainably-managed forest and containing minimum 30% recycled content; and

2) use an environmentally-preferable format including black and white printing instead of colour printing, printing double sided/duplex, using staples or clips instead of cerlox, duotangs or binders.

Via Bid Receiving Unit

Any bid not submitted via e-mail as above must be delivered to the following address:

Health Canada Bid Receiving Unit
Federal Records Centre Building,
161 Goldenrod Driveway (Loading Dock),
Tunney's Pasture, Ottawa, Ontario K1A 0K9
Attention: Cathy Jones
RFP Reference Number: 1000222004
Hours of Operation: 07h30 to 16h30 Monday to Friday

The RFP Reference Number and the name of the RFP Authority must be marked on all documents, binders and respective envelopes.

Due to the nature of the Request for Proposal, transmission of offers by facsimile will not be accepted.

Section I: Technical Bid

In their technical bid, Bidders should demonstrate their understanding of the requirements contained in the bid solicitation and explain how they will meet these requirements. Bidders should demonstrate their capability and describe their approach in a thorough, concise and clear manner for carrying out the work.

The technical bid should address clearly and in sufficient depth the points that are subject to the evaluation criteria against which the bid will be evaluated. Simply repeating the statement contained in the bid solicitation is not sufficient. In order to facilitate the evaluation of the bid, Canada requests that Bidders address and present topics in the order of the evaluation criteria under the same headings. To avoid duplication, Bidders may refer to different sections of their bids by identifying the specific paragraph and page number where the subject topic has already been addressed.

Section II: Financial Bid

Bidders must submit their financial bid in accordance with the Basis of Payment.

Section III: Certifications

Bidders must submit the certifications and additional information required under Part 5.

3.1.1 Electronic Payment of Invoices – Bid

If you are willing to accept payment of invoices by Electronic Payment Instruments, complete Annex "X" Electronic Payment Instruments, to identify which ones are accepted.

If Annex "C" Electronic Payment Instruments is not completed, it will be considered as if Electronic Payment Instruments are not being accepted for payment of invoices.

Acceptance of Electronic Payment Instruments will not be considered as an evaluation criterion.

PART 4 - EVALUATION PROCEDURES AND BASIS OF SELECTION

4.1 Evaluation Procedures

(a) Bids will be assessed in accordance with the entire requirement of the bid solicitation including the technical and financial evaluation criteria.

(b) An evaluation team composed of representatives of Canada will evaluate the bids.

4.1.1 Technical Evaluation

4.1.1.1 Mandatory Technical Criteria

Mandatory Criteria	Page #	YES	NO
M1. The Bidder must submit a project team including a minimum of: • One (1) Project Manager/Lead; and • One (1) Laboratory Technician **Project Manager credentials** The Bidder must propose the services of one (1) Project Manager to oversee the work as described in the Statement of Work (SOW). The Project Manager must have a PhD in a biological science from a recognized Canadian university, or the equivalent as established by a recognized Canadian educational credentials assessment (ECA) service, if obtained outside of Canada. The Bidder must provide: a) A copy of the Project Manager's education credential b) The Project Manager's curriculum vitae An ECA can be obtained from recognized organizations listed on the websites below: • Immigration and citizenship Canada - Where can I get an ECA? • The Canadian Information Centre for International Credentials **Laboratory Technician credentials and experience** The Bidder must propose the services of one (1) Laboratory Technician to conduct the work as described in the SOW. The Laboratory Technician must have experience in pharmacological assessment for the past 2 years, including experience related to *in vitro* GPCR activation testing and experience reporting pharmacodynamic data. The Laboratory Technician must have experience with the development of robust *in vitro* protocols for pharmacology assessment (1 project completed). This experience must include activities that employed a range of human and animal cell lines (1 project completed). For each proposed project team member, the Bidder must provide the following information on the relevant projects and experience: a) Laboratory Technician name; b) Curriculum vitae (CV); c) Relevant project(s):			

Mandatory Criteria	Page #	YES	NO
i. Short description; ii. Laboratory Technician contribution. Experience gained during a course or formal training will not be considered work experience. All requirements for work experience must be obtained in a legitimate work or academic work environment (e.g. academic laboratory) as opposed to an educational setting (e.g. courses during the completion of a Bachelor of Science degree).			
M2. Experience with *in vitro* pharmacodynamics The Project Manager must have experience in conducting pharmacological testing that involves: a) Measuring Emax[1] and EC_{50}[2] on human G protein-coupled receptors (GPCRs) b) Using these data to compare the *in vitro* activity of various substances The Project Manager must have completed one project of similar scope, size and complexity as the project described in the Statement of Work (SOW) for this Request for Proposals (RFP) within the last 5 years prior to the closing date. The Bidder must provide a summary of 1000 words or less describing the project. The project summary should include: a) Brief description; b) Start and end dates; c) Role of the Bidder; d) Methodology; e) Deliverables; f) If the project was published: a citation and an electronic copy of the publication(s); g) If the project was not published: a reference with current telephone number and/or email address for each project for verification purposes. Experience gained during a course or formal training shall not be considered work experience. All requirements for work experience shall be obtained in a legitimate work or academic work environment (e.g. academic laboratory) as opposed to an educational setting (e.g. courses during the completion of a Bachelor of Science degree).			
M3. Scientific publications The Project Manager must have experience publishing original scientific research in peer-reviewed journals. The Bidder must provide one (1) example within the last 5 years prior to the closing date. Scientific peer-reviewing is a process by which scientific work is submitted to independent referees – scientific peers in the same field – who will evaluate and provide input on scientific methology, results, and findings prior to publication. Because there is no universal definition of academic peer-review, a publication will be considered peer-reviewed for this proposal if it is indexed in the MEDLINE or EMBASE databases. The Bidder must provide the following information: a) A citation and an electronic copy of the publication; b) A description of the Bidder's or Project Manager's contribution to that publication.			

[1] Emax = maximum effect of GPCR activation

[2] EC_{50} = concentration producing 50% of the maximum effect on GPCR activation

Mandatory Criteria	Page #	YES	NO
The Project Manager must be identified as lead (first) or as a corresponding (last) author on the publication.			
M4. Workplan, schedule, and deliverables The Bidder must include in their technical proposal a detailed workplan listing the specific tasks and deliverables. Major activities must include but are not limited to the following: • Preparation of controls, test substances, and reagents • Cell culture • *In vitro* expression of human Mu Opioid Receptor (hMOR) • *In vitro* quantification of hMOR activation • Data analyses For all major activities, the detailed workplan must provide the following information: a) Individual tasks; b) Personnel assigned to each task; c) Required materials and equipment; d) Proposed schedule for completion or delivery in relation to the requirements of the SOW (sections 3.1 and 5.1).			
M5. Access to resources and equipment The Bidder must provide a summary describing the required equipment and how access is granted in order to prove their readiness to begin the work described in the SOW immediately following contract award. For all equipment listed in the detailed workplan (see M4), the summary must include the following information: a) Make, model; b) Owner of the equipment; For any equipment not owned by the Bidder, the summary must also include the following: c) How access is granted: i. Is it shared or borrowed? ii. Is it rented?; d) Planned schedule for its use (e.g. 3 hours per week for 6 weeks); e) Owner confirmation that the equipment will be available for the specified schedule (email is sufficient).			
M6. Future proofing To demonstrate that the chosen methodology allows to repeat the experiments on an additional number of substances, the Bidder must provide the following information: a) How stable cell lines will be stored; b) How transgenes will be stored (if applicable); c) Are reagents prepared in-house in the laboratory? If a given reagent isn't prepared in-house, is it readily available from commercial sources? d) Will the required equipment be available for future projects?			

4.1.1.2 Point Rated Technical Criteria

	Rated Requirements	Page #	Points allocation	Score
R1	**Experience with in vitro pharmacodynamics** Points will be granted for additional projects of similar scope, size, and complexity as the project described in the SOW for this RFP and completed within the last 5 years prior to the closing date. (Experience already submitted to meet M2 requirements cannot be reused for R1. Consideration will be given to the number of substances and/or receptors tested in individual projects. For example, in relation to as the project described in the SOW for this RFP: projects that evaluated twice as many pharmacological targets would be counted as two (2) projects for this rating; projects that evaluated three (3) times as many test substances would be counted as two (2) projects; and so on.		1 project: 1 pt 2 projects: 2 pts 3 projects: 3 pts 4+ projects: 5 pts	
R2	**Scientific publications** Points will be granted for the number of scientific publications in addition to the example provided in M4 within the last 10 years prior to the closing date. Only publications in peer-reviewed journals will be accepted. Scientific peer-reviewing is a process by which scientific work is submitted to independent referees – scientific peers in the same field – who will evaluate and provide input on scientific methology, results, and findings prior to publication. Because there is no universal definition of academic peer-review, a publication will be considered peer-reviewed for this proposal if it is a research article indexed in the MEDLINE or EMBASE databases. The Bidder must provide the following information: a) A citation and an electronic copy of the publication; b) A description of the Bidder's or Project Manager's contribution to that publication. The Project Manager must be identified as lead (first) or as a corresponding (last) author on the publication.		1 article: 2 pts 2 articles: 4 pts 3 articles : 6 pts 4+ articles : 10 pts	
R3	**Expertise with Mu Opioid Receptor (MOR)** The Project Manager has work experience in conducting MOR pharmacodynamic testing: a) Measuring Emax and EC_{50} on human MOR b) Using these data to compare the *in vitro* MOR activity of various substances The Project Manager must have completed one or more projects of similar scope, size and complexity as the		1 project: 1 pt 2 projects: 2 pts 3 projects: 4 pts 4 projects: 6 pts 5+ projects: 10 pts	

	Rated Requirements	Page #	Points allocation	Score
	project described in the SOW for this RFP within the last 5 years prior to the closing date. Experience already submitted to meet M2 requirements cannot be reused for R3. The Bidder must provide a summary of 1000 words or less describing the project(s): a) Brief description; b) Start and end dates; c) Role of the Bidder; d) Methodology; e) Deliverables; f) If the project was published: a citation and an electronic copy of the publication(s); g) If the project was not published: a reference with current telephone number and/or email address for each project for verification purposes. Experience gained during a course or formal training shall not be considered work experience. All requirements for work experience shall be obtained in a legitimate work or academic work environment (e.g. academic laboratory) as opposed to an educational setting (e.g. courses during the completion of a Bachelor of Science degree).			
R4	**Methodology – biased signaling 1** The Bidder clearly demonstrates that its chosen methodology can directly measure MOR-specific G protein activation and MOR-specific β-arrestin activation. The Bidder must provide substantiated evidence (e.g. peer-reviewed scientific literature). A publication will be considered peer-reviewed for this proposal if it is a research article indexed in the MEDLINE or EMBASE databases. The Bidder must provide a citation and an electronic copy of the publication.		No: 0 pts G protein: 5 pts β-arrestin: 5 pts Both: 10 pts	
R5	**Methodology – biased signaling 2** The Bidder clearly demonstrates that its chosen methodology can characterize and compare multiple specific effector pathways (e.g. Gαi vs Gαo; Gα vs cAMP or potassium channel activation; β-arrestin 1 vs β-arrestin 2; etc.) and/or conditions representing physiological variations in MOR signaling. The Bidder must provide substantiated evidence (e.g. peer-reviewed scientific literature). A publication will be considered peer-reviewed for this proposal if it is a research article indexed in the MEDLINE or EMBASE databases. The Bidder must provide a citation and an electronic copy of the publication.		One effector per signaling pathway (G protein and β-arrestin): 0 pts Two / pathway: 5 pts Three / pathway: 10 pts Four / pathway: 15 pts Five / pathway: 20 pts Six / pathway: 25 pts	

	Rated Requirements	Page #	Points allocation	Score
R6	**Methodology – groupings** The Bidder clearly demonstrates that its chosen methodology can produce pharmacodynamic profiles in order to establish pharmacological groupings (i.e. substances sharing distinct pharmacodynamic effects). The Bidder must provide substantiated evidence (e.g. peer-reviewed scientific literature. A publication will be considered peer-reviewed for this proposal if it is a research article indexed in the MEDLINE or EMBASE databases. The Bidder must provide a citation and an electronic copy of the publication.		Yes: 5 pts No: 0 pts	
R7	**Methodology – physiological effects** The Bidder clearly demonstrates that its chosen methodology can estimate physiological effects from in vitro pharmacological data by linking to other substances showing similar pharmacodynamics. The Bidder must provide substantiated evidence (e.g. peer-reviewed scientific literature). A publication will be considered peer-reviewed for this proposal if it is a research article indexed in the MEDLINE or EMBASE databases. The Bidder must provide a citation and an electronic copy of the publication.		Quantitative estimation of physiological effects: 10 pts Semi-quantitative estimation: 5 pts None: 0 pts	
R8	**Methodology – additional targets** The Bidder demonstrates capacity to conduct future work with additional pharmacological targets (e.g. KOR, DOR, GABA receptor modulation, monoamine transporters, etc.). The Bidder must provide substantiated evidence (e.g. peer-reviewed scientific literature). A publication will be considered peer-reviewed for this proposal if it is a research article indexed in the MEDLINE or EMBASE databases. The Bidder must provide a citation and an electronic copy of the publication.		Opioid receptors: + 5 pts GABAR modulation: +5 pts DAT/NET/SERT inhibition: +5 pts Monoamine release: +5pts Etc.	
R9	**Methodology – pharmacokinetics** The Bidder demonstrates capacity to conduct future work that includes testing pharmacokinetic properties. The Bidder must provide substantiated evidence (e.g. peer-reviewed scientific literature. A publication will be considered peer-reviewed for this proposal if it is a research article indexed in the		Yes: 5 pts No: 0 pts	

	Rated Requirements	Page #	Points allocation	Score
	MEDLINE or EMBASE databases. The Bidder must provide a citation and an electronic copy of the publication.			
R10	**Licenses or exemptions** The Bidder holds current and up-to-date licenses or exemptions to conduct all required experiments on fentanyls and on morphine. The Bidder must provide substantiated proof of licensing. Licenses and exemptions are issued by Health Canada's Office of Controlled Substances. The application form for an exemption to use a controlled substance for scientific purposes can be found on this webpage: https://www.canada.ca/en/health-canada/services/health-concerns/controlled-substances-precursor-chemicals/exemptions/application-form-exemption-use-controlled-substance-scientific-purposes.html		Yes: 5 pts No: 0 pts	
			Total points	
			Total points available: 100	
			Minimum pass mark: 35 points	

4.1.2 Financial Evaluation

4.1.2.1 Mandatory Financial Criteria

SACC Manual Clause A0220T (2014-06-26), Evaluation of Price

#	Mandatory Financial Criteria	Met (Yes/No)	Cross-Reference to bid *(indicate page #)*
MF1	The bidder's financial bid must not exceed $79,100.00 CAD, including all applicable taxes and travel and living expenses.		

4.2 Basis of Selection

To be declared responsive, a bid must:

a) meet all the mandatory requirements of this solicitation;
b) obtain the required minimum pass marks (35pts) for the Rated Requirements Score; and
c) not exceed Health Canada's budgetary limit on spending for this project: $79,100 CAD.

Proposals not meeting (a), (b), or (c) above will be given no further consideration. Neither the compliant proposal that scores the highest number of rated points nor the one that contains the lowest price will necessarily be accepted.

The contract will be awarded based on “best value,” taking into account both technical merit and price. An asymmetrical weighting has been established whereby technical merit will be valued at 70% of the bid and price at 30%.

Bidder ranking:

For the purpose of ranking all technically acceptable proposals, the following ratio will factor the technical and the price component to establish a total percentage score:

$$\text{Technical Score} = \frac{\text{Bidder's Rated Score}}{\text{Maximum Score}} \times 70\%$$

$$\text{Cost Score} = \frac{\text{Lowest Bid (\$)}}{\text{Bidder's Cost (\$)}} \times 30\%$$

Total Score = Technical Score + Cost Score.

The compliant proposal achieving the highest Total Score will be recommended for award of contracts.

PART 5 – CERTIFICATIONS AND ADDITIONAL INFORMATION

Bidders must provide the required certifications and additional information to be awarded a contract.

The certifications provided by Bidders to Canada are subject to verification by Canada at all times. Unless specified otherwise, Canada will declare a bid non-responsive, or will declare a contractor in default if any certification made by the Bidder is found to be untrue whether made knowingly or unknowingly, during the bid evaluation period or during the contract period.

The Contracting Authority will have the right to ask for additional information to verify the Bidder's certifications. Failure to comply and to cooperate with any request or requirement imposed by the Contracting Authority will render the bid non-responsive or constitute a default under the Contract.

5.1 Certifications Required with the Bid

Bidders must submit the following duly completed certifications as part of their bid.

5.1.1 Integrity Provisions - Declaration of Convicted Offences

In accordance with the Integrity Provisions of the Standard Instructions, all bidders must provide with their bid, **if applicable**, the declaration form available on the Forms for the Integrity Regime website (http://www.tpsgc-pwgsc.gc.ca/ci-if/declaration-eng.html), to be given further consideration in the procurement process.

5.2 Certifications Precedent to Contract Award and Additional Information

The certifications and additional information listed below should be submitted with the bid, but may be submitted afterwards. If any of these required certifications or additional information is not completed and submitted as requested, the Contracting Authority will inform the Bidder of a time frame within which to provide the information. Failure to provide the certifications or the additional information listed below within the time frame provided will render the bid non-responsive.

5.2.1 Integrity Provisions – Required Documentation

In accordance with the section titled Information to be provided when bidding, contracting or entering into a real property agreement of the Ineligibility and Suspension Policy (http://www.tpsgc-pwgsc.gc.ca/ci-if/politique-policy-eng.html), the Bidder must provide the required documentation, as applicable, to be given further consideration in the procurement process.

5.2.2 Federal Contractors Program for Employment Equity - Bid Certification

By submitting a bid, the Bidder certifies that the Bidder, and any of the Bidder's members if the Bidder is a Joint Venture, is not named on the Federal Contractors Program (FCP) for employment equity "FCP Limited Eligibility to Bid" list available at the bottom of the page of the Employment and Social Development Canada (ESDC) - Labour's website (https://www.canada.ca/en/employment-social-development/programs/employment-equity/federal-contractor-program.html#).

Canada will have the right to declare a bid non-responsive if the Bidder, or any member of the Bidder if the Bidder is a Joint Venture, appears on the "FCP Limited Eligibility to Bid" list at the time of contract award.

5.2.3 Status and Availability of Resources

The Bidder certifies that, should it be awarded a contract as a result of the bid solicitation, every individual proposed in its bid will be available to perform the Work as required by Canada's representatives and at the time specified in the bid solicitation or agreed to with Canada's representatives. If for reasons beyond its control, the Bidder is unable to provide the services of an individual named in its bid, the Bidder may propose a substitute with similar qualifications and experience. The Bidder must advise the Contracting Authority of the reason for the substitution and provide the name, qualifications and experience of the proposed replacement. For the purposes of this clause, only the following reasons will be considered as beyond the control of the Bidder: death, sickness, maternity and parental leave, retirement, resignation, dismissal for cause or termination of an agreement for default.

If the Bidder has proposed any individual who is not an employee of the Bidder, the Bidder certifies that it has the permission from that individual to propose his/her services in relation to the Work to be performed and to submit his/her résumé to Canada. The Bidder must, upon request from the Contracting Authority, provide a written confirmation, signed by the individual, of the permission given to the Bidder and of his/her availability. Failure to comply with the request may result in the bid being declared non-responsive.

5.2.4 Education and Experience

SACC Manual clause A3010T (2010-08-16) Education and Experience

The Bidder certifies that all the information provided in the résumés and supporting material submitted with its bid, particularly the information pertaining to education, achievements, experience and work history, has been verified by the Bidder to be true and accurate. Furthermore, the Bidder warrants that every individual proposed by the Bidder for the requirement is capable of performing the Work described in the resulting contract.

PART 6 - RESULTING CONTRACT CLAUSES

The following clauses and conditions apply to and form part of any contract resulting from the bid solicitation.

6.1 Security Requirements

There is no security associated with this requirement.

6.2 Statement of Work

The Contractor must perform the Work in accordance with the Statement of Work at Annex "A".

6.3 Standard Clauses and Conditions

All clauses and conditions identified in the Contract by number, date and title are set out in the Standard Acquisition Clauses and Conditions Manual (https://buyandsell.gc.ca/policy-and-guidelines/standard-acquisition-clauses-and-conditions-manual) issued by Public Works and Government Services Canada.

6.3.1 General Conditions

2010C 2020-05-28, General Conditions - Services (Medium Complexity) apply to and form part of the Contract.

6.3.2 Supplemental General Conditions

Canada to Own Intellectual Property Rights in Foreground Information (2010-08-16) 4007

Health Canada has determined that any intellectual property rights arising from the performance of the Work under the resulting contract will belong to Canada, for the following reasons, as set out in the *Policy on Title to Intellectual Property Arising Under Crown Procurement Contracts*:
the main purpose of the Contract, or of the deliverables contracted for, is to generate knowledge and information for public dissemination.

6.4 Term of Contract

6.4.1 Period of the Contract

The Period of the Contract is from date of Contract Award to May 31st, 2021 inclusive.

6.5 Authorities

6.5.1 Contracting Authority

The Contracting Authority for the Contract is:

Name: Cathy Jones
Title: Senior Procurement Officer
Material Asset Management Division
Chief Financial Officers Branch
Health Canada

11th Floor, 200 Eglantine Driveway,
Tunney's Pasture, Ottawa, ON K1A 0K9
Telephone: 613-298-8295
E-mail address: Cathy.Jones@canada.ca

The Contracting Authority is responsible for the management of the Contract and any changes to the Contract must be authorized in writing by the Contracting Authority. The Contractor must not perform work in excess of or outside the scope of the Contract based on verbal or written requests or instructions from anybody other than the Contracting Authority.

6.5.2 Project Authority – TBA at Contract Award

The Project Authority for the Contract is:

Name: _____
Title: _____
Organization: _____
Address: _____

Telephone: ___ ___ _____
Facsimile: ___ ___ _____
E-mail address: _____

The Project Authority is the representative of the department or agency for whom the Work is being carried out under the Contract and is responsible for all matters concerning the technical content of the Work under the Contract. Technical matters may be discussed with the Project Authority, however the Project Authority has no authority to authorize changes to the scope of the Work. Changes to the scope of the Work can only be made through a contract amendment issued by the Contracting Authority.

6.5.3 Contractor's Representative – TBA at Contract Award

6.6 Proactive Disclosure of Contracts with Former Public Servants

By providing information on its status, with respect to being a former public servant in receipt of a *Public Service Superannuation Act* (PSSA) pension, the Contractor has agreed that this information will be reported on departmental websites as part of the published proactive disclosure reports, in accordance with Contracting Policy Notice: 2012-2 of the Treasury Board Secretariat of Canada.

6.7 Payment

6.7.1 Basis of Payment

The Contractor will be paid for the Work performed, in accordance with the Basis of payment at Annex B, to a limitation of expenditure of *$*_____ **(***insert the amount at contract award***)**. Customs duties and Applicable Taxes are *included.*

No increase in the liability of Canada or in the price of the Work specified in the authorized task authorization resulting from any design changes, modifications or interpretations of the Work will be authorized or paid to the Contractor unless these design changes, modifications or interpretations have been authorized, in writing, by the Contracting Authority before their incorporation into the Work.

6.7.2 Limitation of Price

Canada will not pay the Contractor for any design changes, modifications or interpretations of the Work unless they have been approved, in writing, by the Contracting Authority before their incorporation into the Work.

6.7.3 Method of Payment

The schedule of milestones for which payments will be made in accordance with the Contract is as follows:

Milestone	Description of work	Funding
Anticipated Start Date	**August 1st 2020**	
	Project Authority • Providing a quote for purchasing controls and test substances	N/A
Phase I	**August 1st – September 25th 2020** Contractor • The week of August 10th: the Contractor will provide an invoice for all the materials needed for Phase I. This amount cannot exceed 25 % of the contract value. • Provide a detailed schedule of work with timelines and costs • Ensuring all required licenses are up to date (section 3.1.1) • Ensuring all required equipment is ready and available for use • Obtaining all required materials including cell lines, cell culture media, testing reagents, testing kits, etc. (section 3.1.2) • The Contractor is responsible for purchasing controls (section 6, table I) and test substances (section 6, table II) *Teleconference 1 (the week of September 21st, 2020)*: informing on the status of the project .	The Contractor will report a detailed breakdown of the costs and the total amount for this phase will be provided
	September 28th – October 30th 2020 Contractor • Validating the methodology (section 3.1.3) • If the Contractor provides validation using peer-reviewed literature, the Contractor shall inform the Project Authority (report and teleconference) and then proceed to Phase 3 *Interim report 1*: method validation, This report will be provided one week prior to the teleconference 2. *Teleconference 2* (*the week of October 26th, 2020)*: informing on the status of the project.	The Contractor will report a detailed breakdown of the costs and the total amount for this phase will be provided

Phase II	**November 2nd 2020 – January 29th 2021**
	Contractor
	• Laboratory testing of in vitro MOR activation (Emax, EC_{50}) that includes the following:
	  ○ Determination of full vs partial activation, antagonism, absence of activation
	  ○ Discrimination between inhibitory G protein (Gαi/o) vs β-arrestin effector pathways
	• Experiments must be conducted with a minimum of 6 replicates per control or test substance (section 3.1.4)
		The Contractor will report a detailed breakdown of the costs and the total amount for this phase will be provided

Milestone	Description of work	Funding
	Interim report 2: preliminary results, quality control. This report will be provided one week prior to the teleconference 3. *Teleconference 3 (the week of January 25th, 2021)*: informing on the status of the project, need to repeat experimental measurements (if applicable). The Contractor will provide an invoice following this meeting.	
Phase III	**February 1st – April 1st 2021** <u>Contractor</u> • Drafting a report describing the methodology in detail and tabulated results (section 3.1.5), including but not limited to : o Raw experimental data o Quantitative and statistical analyses o Discussion of the findings o Important considerations o Conclusions • Submission of draft report to the Project Authority for review by March 1st 2021 at the latest *Draft summary report*: see above. This report will be provided one week prior to the teleconference 4. *Teleconference 4* (*the week of March 29nd, 2021)*: discussion on results and the draft summary report. The Contractor will provide an invoice following this meeting.	The Contractor will report a detailed breakdown of the costs and the total amount for this phase will be provided
Phase IV	**April 6th – 16th 2021** <u>Project Authority</u> • Reviewing the draft summary report • Providing comments and input to the Contractor within 5 business days (section 3.1.6) *Input for draft summary report*: see above. To be provided to the Project Authority no later than April 16th, 2021. *Teleconference 5* (if necessary to be held within 2 business days of the submission of comments): discussion on summary report and Project Authority input.	N/A
	April 19th – 30th 2021 <u>Contractor</u> • Incorporating Project Authority input to the final report • Conducting additional analyses (if applicable) • Providing the final report to the Project Authority by March 23rd 2021 at the latest (section 3.1.6) *Final report:* to be provided to the Project Authority no later that April 30th, 2021. The Contractor will provide an invoice with the delivery of the final report. *Teleconference 6 (if necessary, to be held within 2 business days of receipt of the final report)*: discussing final report	The Contractor will report a detailed breakdown of the costs and the total amount for this phase will be provided
Phase V	**May 3rd – 10th 2021** <u>Project Authority</u> • Payment for the contract upon completion of work.	Remainder of funds to be dispersed

Except for the first payment, funds will be allocated upon completion of each phase. The Project Authority can provide up to 25% of the total funding for substances, reagents, materials, and equipment at the

beginning of Phase 1. The remainder of the costs related to this contract will not exceed 25 % in Phases II and III (see table below) inclusively. The Project Authority will therefore provide the remainder of the funds (50 % of the contract value) after the final report has been received in Phase V.

6.8 Invoicing Instructions

The Contractor must submit invoices in accordance with the section entitled "Invoice Submission" of the general conditions. Invoices cannot be submitted until all work identified in the schedule of milestones is completed.

Invoices must be distributed as follows:

One (1) copy must be forwarded to the following email address for certification and payment. hc.p2p.east.invoices-factures.est.sc@canada.ca

If by regular mail: Accounting Operations East - P2P Invoices,, Ottawa, Ontario, K1A 0K9
deposit and Both Health Canada and the Public Health Agency of Canada have adopted electronic direct deposit as their preferred method for paying invoices. Suppliers are encouraged to register for electronic direct to provide their account information upon request.

6.9 Certifications and Additional Information

6.9.1 Compliance

Unless specified otherwise, the continuous compliance with the certifications provided by the Contractor in its bid or precedent to contract award, and the ongoing cooperation in providing additional information are conditions of the Contract and failure to comply will constitute the Contractor in default. Certifications are subject to verification by Canada during the entire period of the Contract.

6.10 Applicable Laws

The Contract must be interpreted and governed, and the relations between the parties determined, by the laws in force in Ontario.

6.11 Priority of Documents

If there is a discrepancy between the wording of any documents that appear on the list, the wording of the document that first appears on the list has priority over the wording of any document that subsequently appears on the list.

(a) the Articles of Agreement;
(b) the supplemental general conditions – (2010-08-16) 4007 – Crown to Own the IP
(c) the general conditions 2010C 2020-05-28;
(d) Annex A, Statement of Work
(e) Annex B, Security
(f) Annex C, Electronic Payment
(g) the Contractor's bid dated _____ (*insert date of bid)*

ANNEX "A"

STATEMENT OF WORK

1. TITLE

Mu Opioid Receptor (MOR) activity profile testing for fentanyl analogues

2. SCOPE

2.1. Introduction

Fentanyl is a synthetic opioid analgesic with a preferential specificity for the μ-opioid receptor (MOR). Upon absorption it is rapidly transported to the central nervous system where it exerts analgesia at therapeutic dosage. At higher doses it can produce euphoria as well as severe physiological effects such as life-threatening respiratory depression. Depending on the route of administration, fentanyl has a potency 50-100 times greater than morphine in humans. Due to its high potency and easy synthesis, fentanyl is contaminating the Canadian illegal drug supply and is responsible for numerous opioid-related deaths. Fentanyl analogues of varying potencies (e.g. carfentanil, furanylfentanyl, acetylfentanyl, etc.) have also entered the illegal drug market and could also pose serious health risks to Canadians. Very little information is known about the effects of fentanyl analogues and the data is mostly limited to those of pharmaceutical interest (e.g. sufentanil, alfentanil, carfentanil).

It is well known that various opioids produce different physiological responses. Part of it is due to specificity with respect to the different opioid receptors. Activation of the μ opioid receptor (MOR) by different substances also results in a range of effects due to variation in how the two major MOR signaling cascades (e.g. G-protein vs. β-arrestin) are triggered. Analgesia is thought to mainly result from G-protein pathways whereas euphoria, dependence, constipation, and respiratory depression are associated with β-arrestin signaling. Relative to morphine, fentanyl has been shown to produce stronger activation of the β-arrestin cascades, leading to a higher potential for abuse and a higher risk of respiratory depression. This phenomenon is known as signaling bias.

Therefore, a key objective of this project is to evaluate the activity of fentanyl analogues and other synthetic opioids at the MOR, but also to investigate their activity on both μ-opioid signaling pathways. There is evidence that structurally similar substances present similar activation profiles and that these correlate with effects reported in humans.

In Canada, the Controlled Drugs and Substances Act (CDSA) provides a legislative framework for the control of substances that can alter mental processes and that may cause harm to the health of an individual or to society when misused or diverted to the illicit market. Activities with controlled substances such as possession, trafficking, import, export and production are prohibited and are punishable offenses except when authorized under regulation. Currently, substances controlled under the CDSA are organized into Schedules I-VI and approximately 350 substances are listed specifically. For a substance that is not listed specifically, in one of the Schedules to the CDSA, Health Canada's Science Division within the Office of Drug Policy and Science (ODPS; the Project Authority) is responsible for conducting a scientific assessment to determine whether this substance is captured under the various listings in the CDSA. Fentanyl and its analogues are controlled under Schedule I, Item 16, of the Canadian Drugs and Substances Act (CDSA). Some but not all analogues are explicitly listed.

In relation to fentanyl analogues the Project Authority evaluates the controlled status of fentanyl analogues under the CDSA and has recently published a fentanyl core-structure that outlines the criteria related to the regulatory decision making for this class of substances. To substantiate the regulatory decision making related to these substances as well as improving our knowledge on

the physiological effects of novel fentanyl analogues, we are proposing an experimental design to evaluate the MOR activity for novel fentanyl analogues and other non-fentanyl synthetic opioids in order to establish a predictive model for human potency and toxicity.

Thus, the purpose of this project is therefore to generate MOR activation profiles for a range of novel fentanyl analogues and well as novel non-fentanyl synthetic opioids and compare the results with known controls, positive (e.g. fentanyl, carfentanil, sufentanil) or negative (e.g. naloxone). This information would strengthen current regulatory decision making and inform the government's efforts with respect to evaluating novel synthetic opioids.

2.2. Objectives of the Requirement

The laboratory testing of fentanyl analogues will provide scientific confirmation whether the substances of interest activate the MOR, but also provide insight on their predicted biological effects. This will support ODPS's regulatory interpretation of the Controlled Drugs and Substances Act with respect to novel fentanyl analogues and other novel synthetic opioids. In addition, the information obtained will allow estimating the real-world potency of fentanyl analogues, which could be useful for the ODPS's law enforcement partners.

2.3. Background and Specific Scope of the Requirement

Fentanyl is a synthetic opioid analgesic with a preferential specificity for the μ-opioid receptor (MOR), as well as a distinctive biased signaling profile associated with abuse and overdose characteristics. Little information is known about the pharmacological effects of novel fentanyl analogues or novel synthetic opioids. This testing contract allows ODPS to gain valuable information related to these substances thus strengthening future regulatory decision making.

3. REQUIREMENTS

3.1. Tasks, Activities, Deliverables and/or Milestones

A summary of activities, deliverables, and timelines is tabulated in section 5.

3.1.1. Licensing requirements

The Contractor shall procure or update all licenses required for the purchasing, storage, and use of test substances and controls (section 6.1, tables I and II).

Expected completion timeline: August-September 2020

3.1.2. Materials and equipment

The Contractor shall have access to or purchase all the necessary experimental equipment, materials, reagents, cell lines, test substances, and controls before beginning the testing. Controls and test substances are listed in section 6, tables I and II.

Equipment should be serviced and calibrated according to the manufacturer's specifications. If equipment is found to be out of specification, full performance test results, in the as-received condition, must be obtained before any adjustment or repair action is taken. On completion of the calibration work, the Contractor shall provide a certificate of calibration signed by the manufacturer's authorized representative. Full performance test results – titration of positive and negative controls – are to be provided. Any omissions from the full calibration are to be notified to the Project Authority and shall be agreed in writing before a certificate, clearly annotated "Limited Calibration" is issued. The Contractor shall include a declaration of measurement uncertainty values with all test results.

If supplied with a quote and justification for the amounts required, the Project Authority will advance funds for the purchases of controls and test substances.

Expected completion timeline: August-September 2020

3.1.3. Assay validation

The Contractor shall ensure that the chosen methodology is suitable to measure the full range of MOR activation as described in section 3.1.4 below. Recent peer-reviewed articles describing the same method in scientific journals are acceptable. Otherwise the Contractor shall clearly demonstrate experimental accuracy, precision, resolution and sensitivity with positive and negative controls. The Project Authority may request the Contractor repeats assay validation if it is deemed unsatisfactory (see section 3.1.9).

Expected completion timeline: October 2020

3.1.4. Pharmacodynamic testing

For each control and test substance, the Contractor shall measure the maximum effect (Emax) and the concentration producing 50% of the maximum effect (EC_{50}) on the human MOR in vitro.

The methodology must be adequate to discriminate between partial MOR activation, full MOR activation, and absence of activation.

The Contractor shall also measure MOR signaling bias. In other words, the methodology must allow to discriminate effects stemming from the two main MOR response pathways:

- inhibitory G proteins (Gαi/o);
- β-arrestins.

The Contractor must perform experiments in triplicate, twice (6 replicates minimum).

Adenylyl cyclase and potassium channel activity may be used to estimate G protein signaling. Additional pharmacological data may be obtained (see Rated Requirements; separate document).

Expected timeline: November 2020 - January 2021

3.1.5. Data analyses and draft report

The Contractor shall draft a report describing the methodology in detail and tabulated results, including but not limited to Emax and EC_{50} values.

The report will also include quantitative and statistical analyses, a discussion of the findings and conclusions, as well as important considerations. Additional relevant analyses (e.g. curve analyses, pharmacodynamics groupings, linkage to known physiological effects, etc.) may be performed as well (see Rated Requirements). The Contractor shall provide all the data and all the analyses in a summary report.

The Contractor will submit the draft report to the Project Authority for review by March 22, 2021 at the latest.

Expected completion timeline: March 22, 2021

3.1.6. Final report

The draft summary report will be reviewed by the Project Authority. Comments will be submitted to the Contractor within 9 business days of delivery (April, 2021). The Contractor will incorporate the Project Authority's input and submit a final report on or before April 30, 2021.

The final summary report must include all raw data, quantitative and statistical analyses, a discussion of the findings, important considerations, and conclusions. Additional relevant analyses (e.g. curve analyses, pharmacodynamics groupings, linkage to known physiological effects, etc.), if conducted, must be included as well.

The Contractor is expected to provide an indexed and searchable electronic copy of the report, as well as original electronic files for figures/graphs.

3.1.7.Documentation
The Contractor shall provide all documentation in English.

3.1.8.Sub-contracting
The Contractor shall not hire sub-contractors to perform any or all work detailed in this contract, without specific and prior authorization in writing from the Project Authority. Any plan to do so must be detailed in the proposal.

3.1.9.Unsatisfactory results
If results significantly differ from reasonable expectations, significant divergence is observed between replicates, or something else went wrong, the Project Authority reserves the right to request assays to be repeated. The Contractor shall provide timely progress updates to allow early identification of unsatisfactory assays and provide sufficient time for the Project Authority to review interim data and request repetition of experiments.

3.2. Specifications and Standards

The Contractor will perform the laboratory testing and analyses as discussed above, using a validated methodology (section 3.1.3) for all the controls and test substances (Appendices I-II).

Upon completion of the laboratory procedures, the Contractor will conduct thorough data analyses (section 3.1.5) as would be expected for any experiment intended to be published in a respected scientific journal. The Contractor shall provide all data and analyses, including but not limited to quantitative and statistical analyses, a discussion of the findings, important considerations, and conclusions. Additional analyses, if applicable, must be provided as well.

The Contractor will provide a draft report and a final report to the Project Authority within the timeline indicated in sections 3.1.5 and 3.1.6.

The Project Authority will review the reports and evaluate whether they meet expected standards of quality, and the criteria discussed herein and in Evaluation Criteria (separate document).

Technical, Operational and Organizational Environment
Under the supervision of the Contractor, the work must be conducted by a trained technician, at least MSc. level or with significant experience publishing similar data. Complex analyses should be performed by a post-doctoral level scientist.

All experimental work is to be conducted at the Contractor's laboratory.

3.3. Method and Source of Acceptance

The following requirements (see Evaluation Criteria, Mandatory Requirements) will ensure the Contractor is suitable to undertake the project:

1. The Contractor's experience conducting pharmacological testing, including Emax and EC_{50}, on G protein-coupled receptors (GPCRs) is well substantiated.
2. The Contractor also has experience publishing in peer-reviewed scientific journals.
3. The Project Manager and Laboratory Technician must meet standard credential requirements.
4. The Contractor readily has access to all required equipment to complete the project.
5. The Contractor provides a detailed technical proposal listing specific tasks, deliverables, and timelines.

Additional criteria (see Evaluation Criteria, Point-Rated Requirements) will help select the proposal that best meets the Project Authority's needs. Submissions that clearly demonstrate they meet the following requirement will receive higher marks:

1. The Contractor conducted additional pharmacological projects similar in scope, size, and complexity, but also evaluating MOR pharmacodynamics (e.g. Emax and EC_{50}).
2. The Contractor published additional scientific articles in peer-reviewed journals.
3. The Contractor demonstrates the capacity to expand the methodology to increase the number of substances tested and/or the number of pharmacological targets.
4. The Contractor can directly assess signaling bias at the MOR, preferably on multiple targets per effector pathway.
5. The Contractor demonstrates the capacity to assess small differences in pharmacological effects, and establish groupings based on similarities and differences among tested substances.
6. The Contractor has the capacity to systematically estimate in vivo physiological effects based on in vitro results.

Furthermore,

1. All assays will be performed twice in triplicates (6 replicates), and in parallel to observe any technical variability in technique (e.g. pipetting).
2. All assays will use a minimum 8-point dose curve to determine EC_{50} and Emax. Subsequent analyses may be performed on data if deemed necessary.
3. The data may be expressed as the mean ± SEM from independent experiments as percent effect relative to the standard reference agonist. Additional relevant statistical evaluations and analyses will also be conducted on the data.

3.4. Reporting Requirements

Following the timelines established in section 5.1 (see table below):

i. Phase I:
    1. The week of August 10th, 2020: The Contractor will provide an invoice for all the materials needed for Phase I. This amount cannot exceed 25 % of the contract value.
    2. The week of September 21st, 2020: the Project Authority will hold a teleconference with the Contractor to discuss the status of the project regarding valid license receipts and purchasing of all materials related to Phase I. The Contractor is expected to communicate any potential delays.

ii. Phase II: the week of October 26th, 2020, the Project Authority will hold a teleconference with the Contractor for the latter to provide an update on the project status, and more importantly to confirm the experimental methodology has been validated. The Contractor is expected to communicate any potential delays and emerging issues. One week prior to this meeting the Contractor will provide interim report.

iii. Phase III: the week of January 25th, 2021 the Project Authority will hold a teleconference with the Contractor to confirm the completion of all experimental work, to discuss preliminary results, and determine whether assays need to be repeated (section 3.1.9). One week prior to this meeting the Contractor will provide interim report. The Contractor will provide an invoice following this meeting.

iv. Phase IV:

1. The week of March 29th, 2021, the Project Authority will hold a teleconference with the Contractor to confirm all pharmacological analyses have been completed. The Contractor will communicate a summary of the results, conclusions, and important information. The Contractor is expected to communicate any potential delays and emerging issues. The draft summary report is expected to have been submitted to the Project Authority one week prior to this meeting. The Contractor will provide an invoice following this meeting.

2. The week of April 12th, 2021 (no later than April 16th 2021), the Project Authority will provide written input on the draft summary report and hold a teleconference with the Contractor to discuss these comments if necessary (teleconference will be held within 2 business days of the submission of comments).

3. The Contractor will submit a final report and an invoice for the remaining funds, to the Project Authority no later than April 30, 2021 at 4:00pm. The Project Authority may hold a teleconference with the Contractor to discuss the final report if necessary. Any remaining funding is to be dispersed within a week of project completion.

v. The funds associated with Phases II and III cannot exceed 25 % of the full contract value.

vi. Phase V: payment of the remainder of funds associated with the contract (50 % of the contract value).

Any emerging issues or questions can be communicated by email in between teleconferences.

3.5. Project Management Control Procedures

The Project Authority and the Contractor will communicate via email and teleconferences (see section 3.5 above) to discuss matters related to the contract. The Project Authority will ensure all the outlined project requirements and acceptance criteria are met. Payment will be issued once milestones are achieved (see section 5).

4. ADDITIONAL INFORMATION

4.1. Canada's Obligations

The Project Authority will be responsible for the following:

- Monitoring project deliverables;
- Scheduling teleconferences after each milestone;
- Making payments as per the funding schedule (see section 5.1);
- Providing comments on the draft summary report within 5 business days.

4.2. Contractor's Obligations

- Unless otherwise specified, the Contractor must use its own equipment and software for the performance of this Statement of Work.
- The Contractor must conduct pharmacological testing of all the substances listed in Appendices I-II in the manner described in section 3.1.

- The Contractor must perform robust quantitative and statistical analyses, discuss findings and considerations, then draw conclusions (see section 3.1.5). The Contractor should conduct additional analyses, if relevant and possible.
- The Contractor must maintain effective communication lines throughout the project, as indicated in section 3.4.
- The Contractor must complete the project and provide a draft report and a final report (sections 3.1.5 and 3.1.6) respectively by 4:00pm on March 26th and April 30th, 2021.

4.3. Location of Work, Work site and Delivery Point

All laboratory work is to be conducted at the Contractor's laboratory. Analyses and reports can be performed at the Contractor's preferred workplace.

4.4. Language of Work

The Contractor shall provide all data and documentation, and should communicate with the Project Authority in English.

5. PROJECT SCHEDULE

5.1. Schedule and Estimated Level of Effort (Work Breakdown Structure) *(if applicable)*

Milestone	Description of work
Anticipated Start Date	**August 1st 2020**
	Project Authority • Providing a quote for purchasing controls and test substances
Phase I	**August 1st – September 25th 2020** Contractor • The week of August 10th: the Contractor will provide an invoice for all the materials needed for Phase I. This amount cannot exceed 25 % of the contract value. • Provide a detailed schedule of work with timelines and costs • Ensuring all required licenses are up to date (section 3.1.1) • Ensuring all required equipment is ready and available for use • Obtaining all required materials including cell lines, cell culture media, testing reagents, testing kits, etc. (section 3.1.2) • The Contractor is responsible for purchasing controls (section 6, table I) and test substances (section 6, table II) *Teleconference 1 (the week of September 21st, 2020)*: informing on the status of the project .
	September 28th – October 30th 2020 Contractor • Validating the methodology (section 3.1.3) • If the Contractor provides validation using peer-reviewed literature, the Contractor shall inform the Project Authority (report and teleconference) and then proceed to Phase 3 *Interim report 1*: method validation, This report will be provided one week prior to the teleconference 2. *Teleconference 2* (*the week of October 26th, 2020)*: informing on the status of the project.
Phase II	**November 2nd 2020 – January 29th 2021** Contractor • Laboratory testing of in vitro MOR activation (Emax, EC_{50}) that includes the following: o Determination of full vs partial activation, antagonism, absence of activation o Discrimination between inhibitory G protein (Gαi/o) vs β-arrestin effector pathways

Milestone	Description of work
	• Experiments must be conducted with a minimum of 6 replicates per control or test substance (section 3.1.4) *Interim report 2*: preliminary results, quality control. This report will be provided one week prior to the teleconference 3. *Teleconference 3 (the week of January 25th, 2021)*: informing on the status of the project, need to repeat experimental measurements (if applicable). The Contractor will provide an invoice following this meeting.
Phase III	**February 1st – April 1st 2021** <u>Contractor</u> • Drafting a report describing the methodology in detail and tabulated results (section 3.1.5), including but not limited to : o Raw experimental data o Quantitative and statistical analyses o Discussion of the findings o Important considerations o Conclusions • Submission of draft report to the Project Authority for review by March 1st 2021 at the latest *Draft summary report*: see above. This report will be provided one week prior to the teleconference 4. *Teleconference 4* (*the week of March 29nd, 2021)*: discussion on results and the draft summary report. The Contractor will provide an invoice following this meeting.
Phase IV	**April 6th – 16th 2021** <u>Project Authority</u> • Reviewing the draft summary report • Providing comments and input to the Contractor within 5 business days (section 3.1.6) *Input for draft summary report*: see above. To be provided to the Project Authority no later than April 16th, 2021. *Teleconference 5* (if necessary to be held within 2 business days of the submission of comments): discussion on summary report and Project Authority input.
	April 19th – 30th 2021 <u>Contractor</u> • Incorporating Project Authority input to the final report • Conducting additional analyses (if applicable) • Providing the final report to the Project Authority by March 23rd 2021 at the latest (section 3.1.6) *Final report:* to be provided to the Project Authority no later that April 30th, 2021. The Contractor will provide an invoice with the delivery of the final report. *Teleconference 6 (if necessary, to be held within 2 business days of receipt of the final report)*: discussing final report
Phase V	**May 3rd – 10th 2021** <u>Project Authority</u> • Payment for the contract upon completion of work.

6. APPLICABLE DOCUMENTS AND GLOSSARY

6.1. Applicable Documents

Table 1. Controls

Substance	CAS #	Estimated cost for 100 µg ($CAD)
Fentanyl	1443-54-5	33
Carfentanil	59708-52-0	118
Sufentanil	56030-54-7	86
Alfentanil	69049-06-5	86
Naloxone	357-08-4	86
Morphine	6211-15-0	52

Table 2. Test substances

Substance	CAS #	Estimated cost for 100 µg ($CAD)
Benzoylfentanyl	2309383-15-9	129
Cyclopropyl fentanyl	1169-68-2	86
para-Methyl cyclopropyl fentanyl	N/A	86
ortho-Methylfentanyl	1443-53-4	86
meta-Methylfentanyl	1465-22-1	78
ortho-Fluorofentanyl	910616-29-4	86
meta-Fluorofentanyl	90736-22-4	86
Thiofentanyl	79278-88-9	86
Beta-methylfentanyl	1443-43-2	86
4-Anilino-N-phenethylpiperidine	21409-26-7	78
Acetyl fentanyl	117332-89-5	47
Butyrylfentanyl	1443-52-3	52
Isobutyrfentanyl	117332-90-8	86
Crotonylfentanyl	760930-59-4	86
Furanyl fentanyl	101365-56-4	86
N-methylnorfentanyl	24775-71-1	86
para-Fluorobutyryl fentanyl	244195-31-1	86
para-Fluroroisobutyryl fentanyl	244195-32-2	86
Methoxyacetyl fentanyl	101365-54-2	86
Benzylfentanyl	5156-58-1	86
AP-237	17730-82-4	86
2-Methyl-AP-237	98608-59-4	86
Etonitazene	911-65-9	100
Metonitazene	14680-51-4	100
UF-17	78866-22-5	86
furanyl UF-17	N/A	86
3'-Methylfentanyl	1082721-49-0	86
N-ethyl-U-47700	N/A	127
3,4-difluoro U-47700	2417942-54-0	86

ANNEX "B"

THERE IS NO SECURITY REQUIRED FOR THIS RFP

Unscreened contractors must be escorted:

1. Unscreened contractors must be escorted by an employee or Commissionaire at all times when visiting GoC facilities.

2. Information which is to be used in the development of the contracted product, as reference material or otherwise made available to the contractor must be unclassified material and considered to be releasable to the public by HC/PHAC and/or The Government of Canada.

3. No Protected or Classified information is to be made available to the contractor, used in the production of the contracted product, or produced as a result of this contract.

ANNEX "C" to PART 3 OF THE BID SOLICITATION

ELECTRONIC PAYMENT INSTRUMENTS

The Bidder accepts any of the following Electronic Payment Instrument(s):

( ) VISA Acquisition Card;
( ) MasterCard Acquisition Card;
( ) Direct Deposit (Domestic and International);
( ) Electronic Data Interchange (EDI);
( ) Wire Transfer (International Only);
( ) Large Value Transfer System (LVTS) (Over $25M)