Call for partners

for the

Global commercialization of a core antigen rapid diagnostic test (cAg RDT) for hepatitis C virus (HCV) infection with a focus on low- and middle-income countries (LMICs)

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CALL FOR PARTNERS

Commercialization of Rapid Diagnostic Test for Hepatitis C Diagnosis

Request for Proposal (RFP) for the global commercialization of a core antigen rapid diagnostic test (RDT) for hepatitis C virus (HCV) infection with focus on low- and middle-income countries (LMIC)

Issue date: Friday, 19 July 2019

RFP Closing date: Friday, 30 August 2019
RFP Closing time: 23:59, Central European Summer Time

Background

It is estimated that 90 million people worldwide are infected with HCV. Advanced liver disease and liver cancer resulting from HCV are responsible for 350,000 to 500,000 deaths each year, making it one of the leading causes of death globally. While rapid tests for HCV screening based on serology exist, limited access to HCV confirmatory testing (i.e., a test to confirm active HCV infection) is one of the major barriers to identifying infected individuals and improving HCV patient management and care.

Currently, there is no fully integrated HCV confirmatory test that can be performed directly from whole blood in target settings. Available molecular assays require stable power supply and temperature control as well as trained operators. The high price of molecular testing is another important barrier to widespread implementation. HCV core antigen (cAg) is a protein marker that is known to be well correlated with HCV RNA levels and therefore can be used in confirmatory testing as an alternative marker of active infection. Based on available evidence, various national and international guidelines have recommended HCV cAg as an alternative to HCV RNA testing. An HCV cAg test in a point-of-care (POC) format would be less expensive, easier to use, and, as a result, a more accessible alternative to HCV RNA tests.

In 2018, FIND went through a process of selecting partners to develop a new rapid lateral flow assay (LFA) platform for detecting HCV cAg. The aim was to prove the feasibility of a product that is affordable and easy to use so that it can be deployed in low infrastructure healthcare settings, thereby improving access to testing for as many individuals with or at risk of HCV infection as possible.

The feasibility stage has been successfully completed and FIND is now planning to continue product optimization and development activities with two product development partners, and is, in parallel, seeking partners with the commercial capability to bring the HCV cAg test to the market.

Final product specifications and rationale

Key product requirements are shown in Appendix I.

Available data on sensitivity limits of lateral flow assay technology suggest that, in this format, an HCV cAg test can provide at best 70-90% clinical sensitivity (50-500 femtomolar (fM) or analytical sensitivity). This test performance is acceptable in the context of a lateral flow HCV cAg test because access to testing is the overriding priority and a testing algorithm can be devised to ensure that all HCV positive individuals are identified and the overall cost to the healthcare system is reduced – see below.

Access to testing will be facilitated by the ease of use and price of an HCV cAg RDT, which can be implemented at lower levels of the healthcare system, thereby enabling further reach to far more patients, including those who are currently not covered by any HCV testing services. The benefits provided by the accessibility of such a test are likely to outweigh its lower sensitivity.

The testing algorithm will be simplified to first conducting a screening test in the form of a rapid HCV serology test that gives a result in 15 min. Next, if the screening test is positive, rapid HCV cAg testing to confirm an active infection would be conducted at the same site and on the same day. If the HCV cAg RDT result is positive, treatment can be initiated on the same visit. If the HCV cAg result is negative, HCV seropositive individuals will be directed to the HCV RNA testing service to ensure that no HCV infected individual is missed. Thus, the HCV cAg RDT will support a test and treat algorithm, under which the majority of HCV-infected individuals will be put on treatment on the same visit. Such an algorithm should greatly decrease loss-to-follow-up. Also, reducing the number of referrals to RNA testing will lower the overall costs to the healthcare system.

NOTE: Performance details for the 2 developed prototypes are available upon request.

Significance

The use of a simple RDT for HCV diagnosis would greatly simplify the algorithms for HCV diagnosis, catalysing an increase in diagnosis rates and treatment scale-up. This effort should ultimately contribute to the WHO targets on HCV for 2030: 80% reduction in incidence, 65% reduction in mortality, and 80% of HCV+ individuals receiving treatment.

Market opportunity

A number of discussions with national and international stakeholders conducted by FIND indicated a great interest in the availability of HCV cAg RDT in LMIC. The majority of stakeholders expressed an opinion that costs and time to result are very important parameters from the public health perspective and that they are willing to accept the trade-off on HCV cAg test clinical sensitivity versus HCV RNA test.
The market size is projected to be 2 - 9 million tests per year three years after launch and 9 - 40 million tests per year five years after launch based on moderate and optimistic market uptake scenarios respectively.

Project scope

FIND invites companies with capacity to manufacture quality assured IVDs (manufacturing can also be offered in collaboration with an appropriate partner), and a global sales, marketing and distribution network in the in vitro diagnostics market, including a commercial presence in LMICs to submit a proposal for the commercialization of the HCV cAg RDT.

Project objectives

1. To conduct a technology transfer from FIND's development partners, at the end of the product development phase.

2. To complete appropriate regulatory studies and submissions in target markets in order to achieve registration in such target markets as well as WHO prequalification.
3. To manufacture the product using their own facilities or in collaboration with an appropriate third party at the required scale to meet market projections while following the necessary quality standards (ISO 13485).
4. To provide commercial sales, marketing and distribution support in target markets. Please, note that all sales revenue of HCV core antigen RDT's would accrue to the commercialisation partner selected.

Eligibility criteria

Companies considering responding to this RFP must meet the following 3 criteria for their proposals to be considered:

1. Have organisational presence in a reasonable selection of LMICs, especially those known to have a high burden of HCV infection
2. Have gained WHO prequalification for at least one IVD product
3. Be willing to commit to an affordable selling price for LMICs, together with other access conditions, to be negotiated as part of the commercialization agreement

Proposals are welcome from organizations with existing in-house capacities for large-scale manufacturing, distribution and marketing as well as from consortiums of two or more entities with established relationships offering to jointly undertake the work. In the latter case, proposal shall be submitted by the lead organization that will be the main point of contact and responsible for further negotiations.

Expected product timelines

The product is expected to be available for transfer to manufacturing at the end of Q2 2020 with manufacturing process defined, pilot manufacturing established and verification testing performed.

Support provided

- Design-locked HCV cAg test ready to be transferred to a manufacturer.
- Exclusive license (royalty-free in LMIC) to manufacture and commercialize the developed core antigen products.

Funding support for development of the Product has been provided to FIND by Unitaid. Where relevant and appropriate, certain terms of Unitaid's funding support to FIND will be applicable to the manufacturer. Such terms will be set out in the Commercialisation Agreement and may include obligations in relation to providing Unitaid with information on progress on commercialisation of the Product and acknowledgement of Unitaid's funding support.

Commercial partner investment

The following typical commercialisation investments will be needed from the selected commercial partner in order to bring the product to the market:

- Carry the cost of transfer of the developed product to their manufacturing operation and scale up (including setting up the manufacturing system, if required).
- Run clinical trials and other studies to obtain regulatory approval in target markets (target markets will be agreed on during contract negotiation process) and WHO Prequalification.
- Ensure adequate manufacturing capacity to meet demand
- Promote the product in the public sector in agreed target markets and submit tender offers for appropriate tenders

- Maintain and manage adequate inventories to meet demand and distribute the product to fulfil orders
- Provide after-sale support, customer training, complaint management

Proposal confidentiality

FIND considers any proposal received under this RFP as confidential. If required, FIND can sign a Confidential Disclosure Agreement (CDA) with interested organizations prior to proposal submission. FIND will not disclose the proposal to third parties without the prior written agreement of the proposal submitter. The review of proposals will be carried out by a team comprising internal FIND experts, independent external experts and potentially also experts from Unitaid. External reviewers (including Unitaid) are under confidentiality agreement and are recused if found to have a potential conflict of interest (which they are obliged to disclose). Any specific questions concerning confidentiality should be addressed to the FIND team.

Proposal content

Expected proposal content is described in Appendix II. Ahead of submission, clarifying questions relating to the RFP content may be directed by email to hcvcoreag@finddx.org. FIND team will respond via email to any request submitted no later than Friday 2 August 2019 at 23:59 Central European Summer Time. All questions and answers will be published on the FIND website by Friday 9 August 2019.

Submission deadline

Proposals must be in English and are to be sent by e-mail to:

hcvcoreag@finddx.org

on or before:

FRIDAY, 30 AUGUST 2019 at 23:59 Central European Summer Time

Selection process

Selection will be based on the submitted proposals. Key criteria for selection are laid out in Appendix III.

Proposals will be assessed and partners selected through a systematic process as described on the FIND website. The process is designed to be objective, independent, and transparent to ensure that the most suitable companies are supported and potential conflicts of interest are avoided.

- Evaluation of proposals will be conducted over a 3-week period following the close of the RFP (up until 13 September 2019). Proposals will be assessed by minimum two internal and two external reviewers based on criteria listed in Appendix II.

- Up to 3 proposals will be shortlisted: shortlisted applicants will be notified by 16 September 2019 and invited to participate in a teleconference call to answer in-depth review questions, and to set up an on-site due diligence visit by a FIND (or FIND-selected) assessor, expected to take place between 16 September 2019 and 19 October 2019. Additional information may be requested by email and will be included in the in-depth review process. Please note that this step will require an independent observer to ensure no undue advantage is given to any of the applicants.

- A decision will be made and communicated to applicants no later than October 31st, 2019.

APPENDIX I: Key product requirements

Attribute	Optimal requirement	Minimal requirement
Platform format	Lateral, vertical, or flow-through immunostrip in cassette format.	
Intended use	1. Diagnose active viraemic HCV infection 2. Confirm active HCV infection after or simultaneously with a positive HCV serology test	
Analyte	HCV core antigen	
Target operator	Community workers with minimal training	
Lowest setting for implementation	Community centres (Level 0)	
Sample type	Capillary whole blood, venous blood, plasma	
Time to result	<10 min (including sample preparation)	<30 min (including sample preparation)
Analytical sensitivity	50 fM core antigen	500 fM core antigen
Analytical specificity	No cross reactivity with endogenous substance and exogenous factors (e.g. HIV-1, HIV-2, HBV, HEV, antimalarials, anti-TB, ART)	
Clinical specificity	>99%	>98%
Genotype inclusivity	Sensitivity and specificity requirements met for genotypes 1 through 6	
Ability to quantitate	Qualitative	
Inter-test reproducibility	Kappa >95%	Kappa >90%

Quality control	Endogenous process control line; tests should be compatible with positive control wells for lot-to-lot QC. Colorimetric indicator to identify excessive heat exposure.	Process control line; tests should be compatible with positive control wells for lot-to-lot quality control (QC).
Sample and reagents preparation	Integrated	Allow for separate sample and reagents preparation disposable (no additional device/instrument). Not more than 5 manual steps required (no precision volume control and precision time steps)
Instrumentation requirements	No instrumentation required	Cassette should be able to run without instrument actuation. Simple reader device to enhance sensitivity and enable automate readings, data analysis (if needed), data storage **Reader Requirements** Small, portable or hand-held, device, ≤5 kg. Battery-operated, and able to run off standard electricity. Designed to pass shock and vibration tests (shipping tests), to have a useful life of 3 years or 20,000 tests in the field and to need preventative maintenance until after 1 year of > 1,000 samples. Capable of storing up to one month's operational and clinical data. With data export and connectivity capabilities. COGS <1,000 (minimum)
Cassette and reagents shipping stability and shelf-life	No cold chain required. Stability at least 12 months at +5 to +40°C. Temperature excursions from -15 to 50°C tolerated for at least 72 hrs.	No cold chain required. Stability at least 12 months at +10 to +35°C. Temperature excursions from -15 to 40°C tolerated for at least 48 hrs.
Assay COGS*	<2 USD	<5 USD

(*) COGS: cost of goods sold, ex-works (not including shipping and distribution margins). FIND is currently conducting impact modelling studies to understand the trade-off between cost and performance. COGS requirements may be adjusted upon completion of these studies.

APPENDIX II: Expected proposal content

Recommended length: 10-15 pages. Supplementary information can be included as appendices for up to an additional 15 pages.

Executive summary (1/2 page)

Organization

- Name and contact detail of main contact
- Brief history of the company
- Public listing (if applicable)
- Financial structure/investor profile
- Legal entity and corporate governance structure
- Total number of employees in the IVD business
- Management structure and biographies of leadership team
- Biographies of senior management who will be directly responsible for commercialization of the HCV cAg test
- Annual revenues in the IVD business
    - Annual revenue growth rate in IVD products
    - Key product areas and geographies driving growth
- Corporate focus/mission
- Strategic fit for an HCV Core Antigen RDT in your current portfolio of products
- Focus on LMIC – percentage of IVD product revenues from LMICs and list of countries with company offices or distributors

Clinical operations and regulatory capabilities

- Number of employees involved in conducting clinical studies and regulatory submissions
- Number of products with regulatory approval (FDA, CE-IVD, WHO prequalification, other e.g. national regulatory approvals in different countries) NOTE: Applicants need to have at least one WHO prequalified product
- Experience with conducting studies and gaining market approval for products in LMIC

Manufacturing Capabilities

- Production capacity for lateral flow devices
    - Antibody and reagent sourcing – make vs buy
    - Injection molding for plastic components
    - Test production and assembly
- Description of any plans to expand production capacity for lateral flow devices
- Location of production facilities worldwide
- Quality certifications for production facilities
- Likely ability to reach a cost of goods of < $2/test for a lateral flow device at scale (>1M tests per annum)
- If manufacturing is offered as part of a collaborative agreement with a partner, please provide the history of the relationship, and information demonstrating successful and reliable product supply.

(Please provide supporting cost structure as well as volume-based cost improvement projections (NOTE: Preliminary estimate of production cost of currently available prototype is available on request)

Commercial organization

- Description of the global commercial organisation structure (sales, marketing, distribution and after sale support)
- Number of countries worldwide with a company-owned local subsidiary/affiliate
- Number of countries worldwide in which the company uses distributors/agents
- Details of the commercial organisation in LMIC in Africa, Asia and Latin America
- Description of relationships with global and national public health organisations (National ministries of health, UNICEF, WHO, UNITAID, PEPFAR, Bill & Melinda Gates Foundation, Clinton Health Access Initiative, FIND, MSF and others). Include previous collaborations and their respective dates.

Distribution and support organization

- Description of global logistics organisation
- Description of product training provided to customers
- Description of complaint handling and correction and preventive action (CAPA) resources available

HCV Core Antigen RDT commercialization plan

- If your company were to commercialise the HCV Core Antigen RDT, what would a rough strategy and plan look like?
    - Key worldwide markets – give rationale
    - Regulatory strategy
    - Likely sales and marketing targets in those markets
    - Likely sales and marketing approach
    - Distribution channels
    - Likely volume-based pricing strategy in LMIC's (Please provide cost structure to support your proposal)
    - After sale support plan

APPENDIX III: Organization assessment criteria

Criterion	Description
Company business model	Alignment of the company's business model with global health, as measured by percentage of IVD product revenues from LMIC's and organisational presence in LMIC's.
Current annual sales	History of sales volumes of lateral flow immunoassay-based point-of-care IVD products the company sells per year in 2016-2018
Financial health	Indicators of the company financial condition
Relationship with global public health organisations	History of collaboration with major Global Health stakeholders, such as Bill & Melinda Gates Foundation, Clinton Health Access Initiative, FIND, Global Fund, MSF, PEPFAR, UNICEF, UNITAID, WHO.
Clinical and regulatory capabilities	Current capacity for running and completing clinical studies and successful product registration
Manufacturing capacity	Current capacity of LFA manufacturing lines
Quality system strength	Certifications, extent of quality systems and experience in regulatory requirements
Relevant IVD products menu	Availability of IVD products for HBV, HCV, HIV, TB, malaria, syphilis
Distribution capacity	Based upon the current distribution and logistics capabilities
Affordable but sustainable pricing in public market in LMIC	Description of the pricing approach/strategy for similar products in LMIC's. In addition please provide a hypothetical scenario, assuming a production cost of $1.80 per complete unit, what price range can be committed to?

APPENDIX IV: Preliminary key term sheet

Access Component	Terms of Agreement
List of deliverables	Commercialization partner will: • lead the process of technology transfer from the development partner to manufacturing • prepare and submit a regulatory dossier for the WHO Prequalification Programme (WHO PQ) and the Global Fund/Unitaid supported Expert Review Panel for Diagnostics (ERPD) • prepare and submit a plan for regulatory filings to appropriate national regulatory authorities for target LMIC markets • prepare and submit a market entry, sales and distribution strategy in line with access commitments agreed to in the Commercialization Agreement • prepare a production and supply plan through 2025 that ensures capacity to supply qualified orders (minimum size to be determined as part of the project plan) with manufacturing lead time of no more than 90 days • promote and distribute the Product according to the sales and distribution strategy presented to reach maximum access for the Product across LMIC markets
Price	• Manufacturer commits to making the Product available to Public Sector Purchasers seeking to supply the Products to the Target Countries at an "Affordable Price". • "Affordable Price" means the lowest, sustainable, competitive price level for the Products. It will cover the cost of raw materials and full production costs and may also include a reasonable margin to help ensure the economic sustainability of production, product promotion, distribution and support in targeted LMIC's. • "Affordable Price" may be determined on the basis of one of the following approaches: (i) Appropriate benchmark price (if an appropriate benchmark exists); or (ii) COGS plus a reasonable margin. • The applicable approach to determining the Affordable Price should be agreed and set out in the Commercialisation Agreement (together with the amount or range of reasonable margin, if applicable). • Final product pricing will be negotiated upon completion of development and successful evaluation trials. Pricing may be a function of manufacturing volumes
Supply Security	• Manufacturer commits to making the Products available in sufficient quantities to meet the needs of the public sector in the Target Countries. This will essentially include a commitment in relation to minimum annual production capacity • A base minimum annual production capacity commitment may be agreed and set out in the Commercialisation Agreement. The Parties may agree to adjust this commitment closer to product launch. • If the Product will also be commercialised in High Income Countries, the Commercialisation Agreement will include an obligation to implement measures to protect volumes destined for Public Sector Purchasers in the Target Countries.

Registration	• Manufacturer commits to making best efforts to registering the Products in Key Countries in a timely manner. • Commercialisation Agreement should include a list of Key Countries and a milestone in relation to determining Regulatory Strategy and timing for registrations in Key Countries.
Public Sector Purchasers	• Manufacturer commits to making the Products available to all Public-Sector Purchasers seeking to supply the products to the Target Countries. • Public Sector Purchasers include: (i) Governments and government agencies (ii) NGOs and technical partners such as MSF, ICRD and UN organisations (iii) Funders such as Unitaid, PEPFAR and the Global Fund
Target Countries	• Manufacturer commits to making the Products available at the Affordable Price to all Public-Sector Purchasers seeking to supply the products to the Target Countries. • Target Countries should be defined (as appropriate) and included in the Commercialisation Agreement.
Management of IP	• IP rights to the HCV cAg RDT product will be held by FIND, and manufacturer will operate under an exclusive license, in exchange for which FIND will require appropriate pricing commitments in LMIC's (note that FIND may select more than one commercialisation partner for the Product, in the event that access requirements agreed in this contract are not met in LMICs).
Measures to Ensure Development of the Product	• If manufacturer is unable to develop the Product or commercialise in accordance with access conditions, FIND may terminate the Commercialisation Agreement and require transfer of any know-how and IP to an alternative manufacturer.
Termination Rights	• Manufacturer agrees that FIND may terminate at any time for no reason on appropriate notice (as required in accordance with Unitaid Standard Terms & Conditions).