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Evaluation of a production ready portable, Point of Need Platform (instrument and reagents), direct from nasal swab test for the molecular diagnostic detection of COVID-19 infection

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« This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101005075. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA »

KRONO MEMBERS

Nelson Nazareth

BGR / BioGene, UK

Nathan Nazareth

David Edge

Rémi Charrel

AMU, France

Margo Barthelemy
Thérèse Atieh
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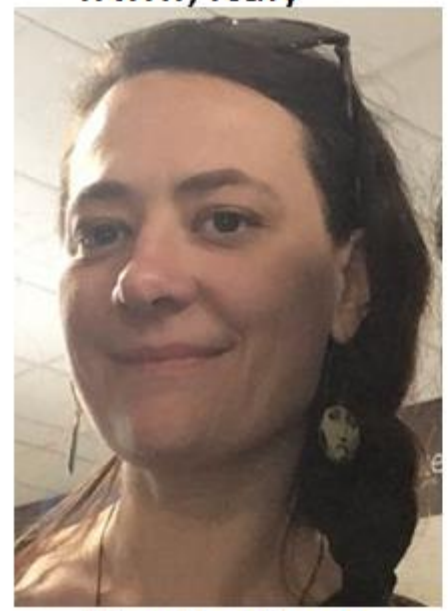
Sandy Gore

Giulia Matusalia

INMI, Italy



Claudia Minosse
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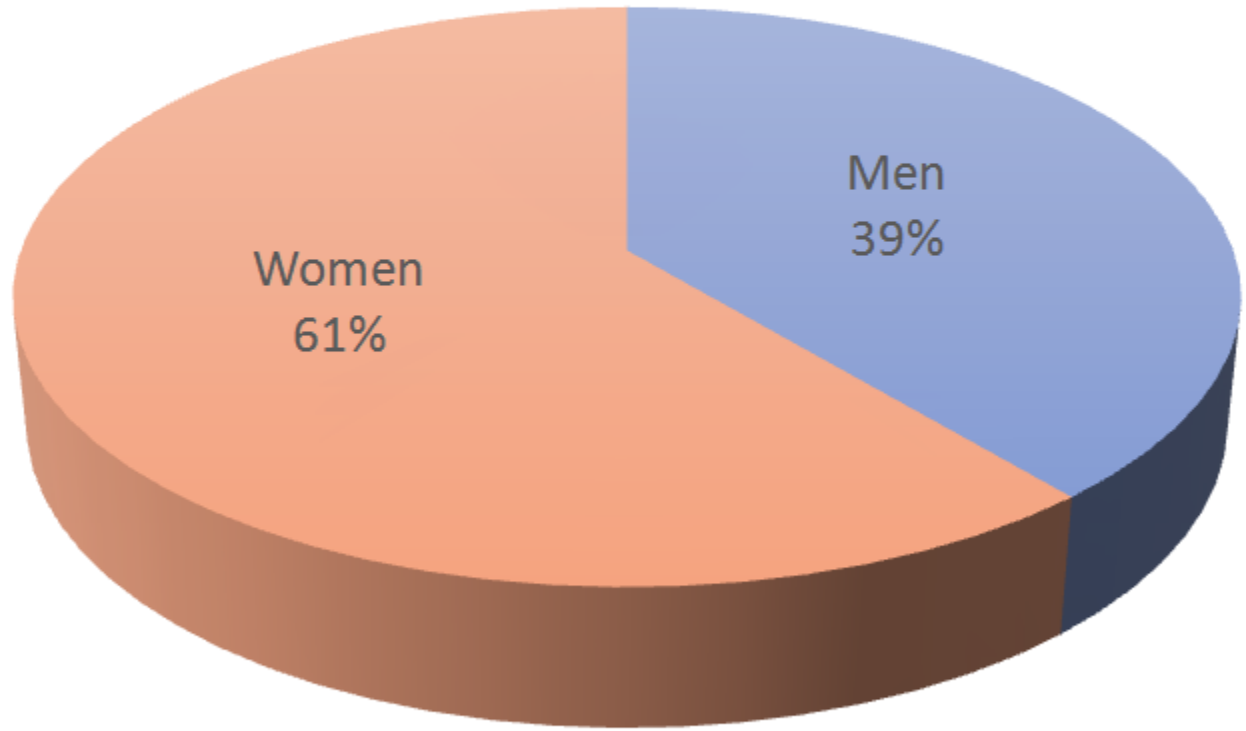
UCPP, France

Lisandru Capai

GENDER

- BGR/BG involve 100% of men (3)
- AMU involve 60% of women (3) and 40% of men (2)
- INMI involve 87,5% of women (7) and 12,5% men (1).
- UCPP involve 50% of women (1) and 50% of men (1)



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Evaluation of a production ready portable, point-of-need platform (instrument and reagents), direct from nasal swab test for the molecular diagnostic detection of COVID-19 infection

Ongoing | IMI2 | Respiratory diseases, Infectious diseases, Coronaviruses, Diagnostics

Summary

Currently, COVID-19 diagnostic tests need to be processed by an expert in a laboratory, and patients often have to wait at least a day for their results. The KRONO project aims to change that by delivering a simple test that can be used at a doctor's office or a patient's home (for example) and would deliver results in just 40 minutes.

The diagnostic kit is based on novel technology that can work with unprocessed samples of blood, saliva, or nose or throat swabs and can be operated by anyone with basic training in how to use the device. The software is based on algorithms trained on actual clinical data, and allows users to easily interpret the results.

While the team is focusing its efforts on the current COVID-19 outbreak, they also plan to ensure the system can be easily adapted to future outbreaks of new diseases in humans as well as animals.

Achievements & News

A rapid diagnostic test 'pipeline' for current and future pathogens

October 2020

KRONO's COVID-19 test technology will make the world more prepared for new threats to human, animal and even plant health

Participants

Show participants on map

Universities, research organisations, public bodies, non-profit groups

- Istituto Nazionale Per Le Malattie Infettive Lazzaro Spallanzani-Istituto Di Ricovero E Cura A Carattere Scientifico, Rome, Italy
- Universite D'Aix Marseille, Marseille, France
- Universite De Corse Pascal Paoli, Corte, France

Small and medium-sized enterprises (SMEs) and mid-sized companies (<€500 m turnover)

- B G Research LTD, Kimbolton, United Kingdom
- Biogene LTD, Kimbolton, United Kingdom

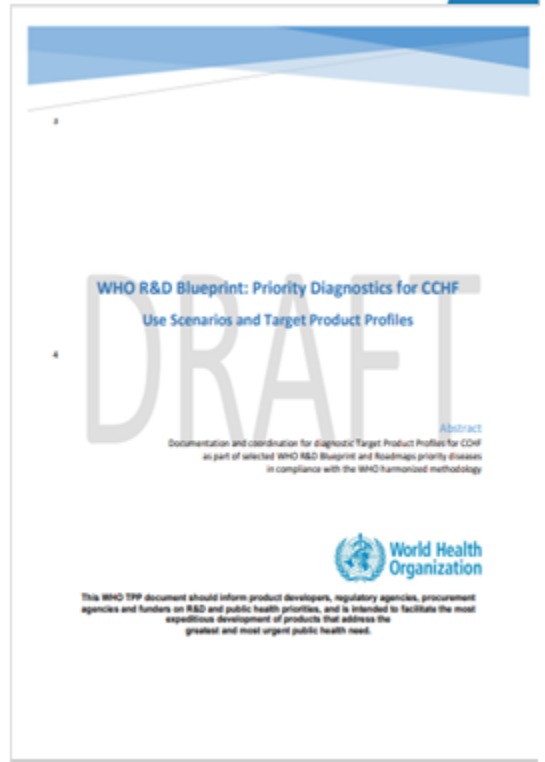
FACTS & FIGURES

Start Date	01/09/2020
End Date	31/12/2021
Call	IMI2 - Call 21
Grant agreement number	101005075

Type of Action:
RIA (Research and Innovation Action)

Contributions	**€**
IMI Funding	784 470
Other	1 035 494
Total Cost	1 819 964

Project coordinator
Rémi Charrel
Universite D'Aix Marseille



KRONO KEY OBJECTIVES

- Meet the WHO R&D blueprint TPP of 10,000 virions/ml detection for simple to use, low cost tests for use in the developing world
- Ability to deploy tests for use without lab access in remote regions and used by anyone with simple training
- Drive the cost of goods to the point that assays can be sold at the price point of lateral flow but with sensitivity of molecular
- Advancement of the portable detection system from the existing lab-based technology demonstrator to a portable validated production unit ready to be manufactured at scale to impact on both the current pandemic and future outbreaks of emergent disease
- Development and validation of the SARS-CoV-2 assay, including internal positive control – latterly becoming a Duoplex test.
- Demonstration of rapid development and scaling to production of the lyophilised assays, including enzyme production, reagent and lyophilisation development

BioGene

BGResearch

QuRapID-XF ONE Application Areas

Ports of Entry and Travel

Proactive Pandemic Preparedness

Screening of Soldiers and FOBs

Border Control and Immigration

Humanitarian Efforts and Aid

Triaging and Treatment

Major Events (e.g. Sporting, Religious and Political)

Deployment in Local GP Surgeries and Care Homes

Veterinary

Containment and Quarantine

Biosecurity and Biowarfare

Homeland Security

PLANNING AND PROJECT MANAGEMENT

- The ISO 13485 QMS gives BG Research a strategic capability in planning and management of projects
- Each project has its own dedicated Design and Development Plan (DDP) where key milestone deliverables and required resources are documented
- A master project Gantt is used to ensure tasks are clearly defined, assigned and completed within specified time frames
- The Gantt is updated on an ongoing basis and a weekly forecast issued each week (forecasted tasks integrated into assigned personnel's daily worksheets)
- Monthly documented team meetings (biology, mechanical and quality) are scheduled at the end of each month (used to summarise work, identify any bottlenecks/risks and plan objectives)

XF1 Reagent System	**493 days**	**Wed 20/11/19**	**Fri 08/10/21**		
RT-PCR Master Mix	**304 days**	**Tue 11/08/20**	**Fri 08/10/21**		
Revisit probe/fluorophore combinations	5 days	Mon 04/10/21	Fri 08/10/21	David Edge [10%]	
Positive Control assay testing	5 days	Mon 20/09/21	Fri 24/09/21	James Turton [10%]	
Buffer	**185 days**	**Mon 11/01/21**	**Fri 24/09/21**		
Saliva and Swab Inhibition Investigation Continued	15 days	Mon 06/09/21	Fri 24/09/21	James Turton [10%]	
Develop buffer without ammonium sulphate	15 days	Mon 16/08/21	Fri 03/09/21	David Edge [10%],James Turton [10%]	
Make new blood buffer based on ammonium acetate	3 days	Wed 15/09/21	Fri 17/09/21	David Edge [10%]	
Make, test and ship latest buffer	10 days	Mon 06/09/21	Fri 17/09/21	James Turton [10%]	
Human Assays	**483 days**	**Wed 20/11/19**	**Fri 24/09/21**		
COVID-19	**343 days**	**Wed 03/06/20**	**Fri 24/09/21**		
VOC/VUI Surveillance	15 days	Mon 06/09/21	Fri 24/09/21	James Turton [10%]	

JAMES TURTON (JT) GANTT TASK LIST
DATE OF UPDATE: Friday 17th September 2021
TASKS FORECAST TO: Friday 24th September 2021

PLEASE DRAG & DROP THIS FORECAST INTO YOUR DAILY WORKSHEET

1. All tasks being worked on must follow and align with the established Gantt
2. All tasks are assigned a unique Gantt Task ID so no task should be marked as N/A unless previously advised or is out of your control
3. The Gantt should be accurate up to 2 weeks minimally (updated every Friday)
4. The % completion of tasks is to be accuratley updated on a daily basis
5. Worksheets are to be updated and sent at the end of each working day
6. Any individual task more than 7 days duration needs to be divided into relevant sub-tasks
7. Justification must be provided if a task is not completed by its scheduled due date
8. Any bottlenecks are to be reported so additional resources can be allocated

Assigned Gantt Tasks	Unique Gantt ID	Project	Task Summary Name	Start	Finish
Saliva and Swab Inhibition Investigation Continued	1296	QuRapID-XF	Buffer	Mon 06/09/21	Fri 24/09/21
VOC/VUI Surveillance	1347	QuRapID-XF	COVID-19	Mon 06/09/21	Fri 24/09/21
Weekly clean and wipe down of laboratories (record on cleaning log)	697	QuRapID-XF	Housekeeping, Cleanliness and Infrastructure Maintenance	Fri 24/09/21	Fri 24/09/21
Weekly cleandown and organisation of workspace/desk	698	QuRapID-XF	Housekeeping, Cleanliness and Infrastructure Maintenance	Fri 24/09/21	Fri 24/09/21
Internal CoV2 Saliva Testing (Monday and Friday)	1020	QuRapID-XF	Housekeeping, Cleanliness and Infrastructure Maintenance	Mon 20/09/21	Fri 24/09/21
Positive Control assay testing	1338	QuRapID-XF	RT-PCR Master Mix	Mon 20/09/21	Fri 24/09/21

1.0 MEETING DETAILS

Department	Quality	**Location**	Boardroom
Month	July	**Date**	30.07.21

	Meeting Attendees	Position
1	Nathan Nazareth	Quality Manager
2	Nelson Nazareth	Managing Director

	Agenda of meeting
1	To summarise months' work and findings
2	To identify risks and implement the necessary controls
3	To discuss the status of objectives set for the current month
4	To discuss and set new objectives for the following month
5	To plan project work and timelines

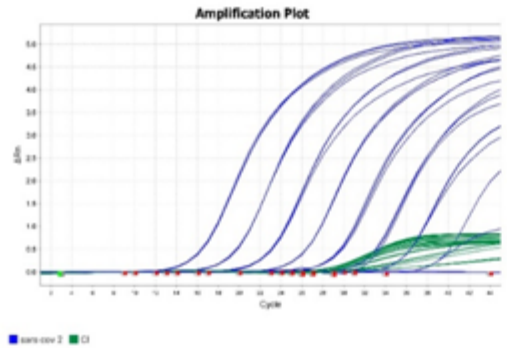
2.0 SUMMARY OF MONTHS WORK, FINDINGS AND GENERAL COMMENTS

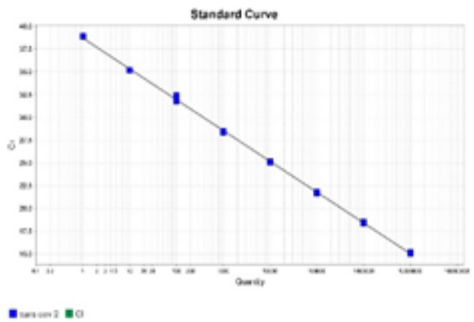
- CIM50 has now been implemented and integrated with the companies live Sage 50 data. Tina has been working on ensuring all data is up to date and has been pulled through from Sage 50 accounts. The training conducted has given a good overview and understanding of how to use the key functions of the software. Once Tina has more experience with he system further training on specific areas will be scheduled with ACIT.
- The new more intuitive BioParts numbering system has been set-up and allows easy identification of parts without having to scan/look them up. The new system has been applied to existing stock on Sage 50 and CIM50.
- Riley automation have been selected to be used for the automation of the barcoding system. They were the most technically competent and competitively priced. However further meetings will be needed to negotiate a full turnkey system which can be run and validated.
- Samples from Edding have been received using the new XF1 reaction vessel. Following testing a key finding was the black printed barcodes seemed to have better readability than the white ones. Using black ink will be simpler and may provide more options in terms of ink types. Both Edding and Domino have been contacted asking what choices there are for black ink (including the possibility of alcohol resistant ink that does not require UV curing). Still awaiting samples from Domino, once received a supplier can be selected for the provision of the printer and ink.
- WHO responded to the pre-submission request asking for questions to be asked and a plan for studies/testing to be conducted as part of the EUL submission. These will need to be confirmed and converted into a document before a pre-submission meeting can be scheduled.

First batch of reagents Experiments to compare BGR reagents vs Altona Kit (by using SARS-CoV-2 extracted RNA)

Altona

	Ct
10^7 cp/reaction	15,129
10^7 cp/reaction	15,150
10^7 cp/reaction	15,012
10^6 cp/reaction	18,410
10^6 cp/reaction	18,373
10^6 cp/reaction	18,492
10^5 cp/reaction	21,783
10^5 cp/reaction	21,659
10^5 cp/reaction	21,778
10^4 cp/reaction	25,095
10^4 cp/reaction	25,032
10^4 cp/reaction	25,106
10^3 cp/reaction	28,481
10^3 cp/reaction	28,397
10^3 cp/reaction	28,313
10^2 cp/reaction	32,421
10^2 cp/reaction	31,925
10^2 cp/reaction	31,745
10 cp/reaction	35,133
10 cp/reaction	35,153
10 cp/reaction	35,132
1 cp/reaction	38,857
1 cp/reaction	Undetermined
1 cp/reaction	38,910
neg	Undetermined
neg	Undetermined
neg	Undetermined



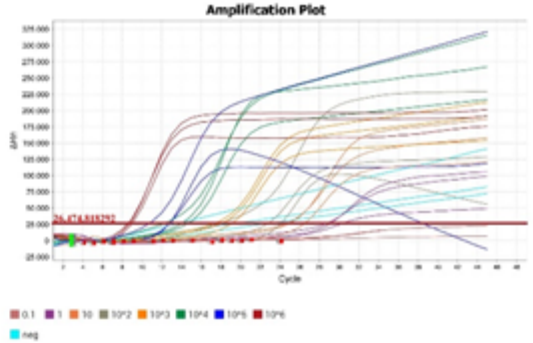


Slope= -3,378
Efficiency= 97,716

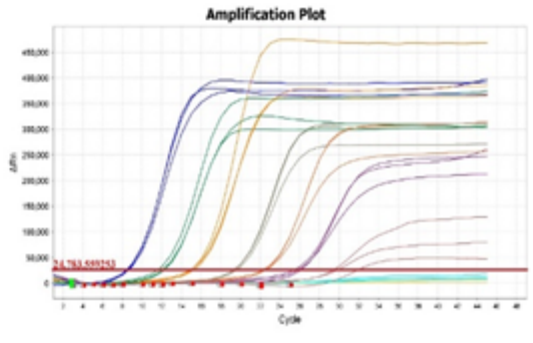
BGR (First batch of reagents)

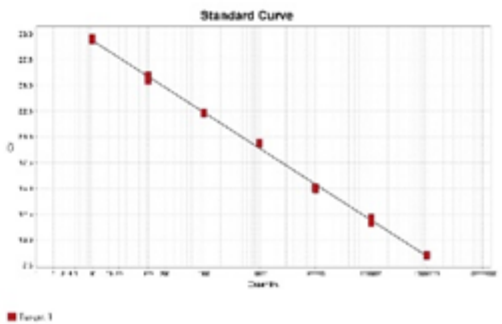
	20 uL Ct	50 uL Ct
10^7 cp/reaction	8,585	8,611
10^7 cp/reaction	8,741	8,412
10^7 cp/reaction	8,955	8,525
10^6 cp/reaction	10,775	12,220
10^6 cp/reaction	12,785	11,551
10^6 cp/reaction	12,802	12,020
10^5 cp/reaction	12,271	14,853
10^5 cp/reaction	14,705	15,192
10^5 cp/reaction	14,094	14,955
10^4 cp/reaction	19,109	19,535
10^4 cp/reaction	17,418	19,256
10^4 cp/reaction	18,135	19,286
10^3 cp/reaction	22,788	22,393
10^3 cp/reaction	24,049	22,462
10^3 cp/reaction	17,898	22,239
10^2 cp/reaction	26,486	25,772
10^2 cp/reaction	24,727	26,031
10^2 cp/reaction	24,993	25,358
10 cp/reaction	29,082	29,293
10 cp/reaction	28,749	31,755
10 cp/reaction	30,352	29,689
1 cp/reaction	Undetermined	Undetermined
1 cp/reaction	Undetermined	Undetermined
1 cp/reaction	Undetermined	Undetermined
neg	22,875	Undetermined
neg	13,748	Undetermined
neg	19,581	Undetermined

20 uL



50 uL





With BGR: Detection up to 10 cp/reaction
Best final reaction volume is 50 uL