INDIAN COUNCIL OF MEDICAL RESEARCH
Department of Health Research - Ministry of Health & Family Welfare
Government of India

Rapid diagnostics for Antimicrobial Resistance (AMR)

ICMR had earlier communicated a brief questionnaire in January, 2019 to you to understand your journey as innovator and the diagnostic test developed by your group. Your experience was helpful to ICMR in understanding the gaps and factors hindering the availability of diagnostics. We want to know whether your diagnostic has move forward/progressed since the time we last spoke to you. We would appreciate if you could spare some time to share your experience and provide information* on following:

S.No	Diagnostic (Dx)	
1	Any change or modification or improvement made in Dx since last ICMR survey (January 31, 2019)	
2	Validation performed for analytical parameters	☐ In-house only/internal ☐ External verification in collaboration with any hospital/research institute/field ☐ Third party/ Independent Evaluation done
3	Any other analytical or performance parameter checked as a part of improvement in diagnostic	Parameters that have been evaluated for Dx as mentioned in response to earlier questionaire (Jan 2019): Sensitivity, specificity, NPV, PPV, LoD, Precision, Linearity, Accuracy, Reproducibility, LoQ If Any Other, Pls mention:
4	Stability /Shelf life tested	☐ Yes ☐No
5	Scalability possible	☐ Yes ☐No
6	Evidence of scalability available	☐ Yes ☐No
7	Whether cost effectiveness study performed and evidence is available	Cost-effectiveness study done ☐ Yes ☐No Evidence available ☐Yes ☐No
8	Whether product reached market	☐ Yes ☐No
9	Technology Readiness Level (TRL) **please see attached annexure for definition of TRL-scale	TRL……
10	Any major challenge or hindrance you feel in the way of Dx availability in the market	

You may withhold sensitive/confidential information.

You may be aware that ICMR has a task-force on the 'Rapid AMR diagnostics' to facilitate the uptake of available AMR diagnostics in healthcare system. The taskforce proposes to…

- Create Target product profiles (TPP) for AMR diagnostics as per requirement of Indian healthcare system;
- Compile validation protocols which can guide innovators/developers of AMR diagnostics through the validation process;
- Undertake field feasibility and cost-effectiveness studies of AMR diagnostics;

Since you have the prior experience of developing such diagnostic, we wish to understand the following from you:

Whether consulted any Target product profiles (TPP) at the time of the Dx development	☐ No ☐ Yes If Yes, tick the applicable ☐ WHO ☐ FIND ☐ Other, Pls specify
Standards/guidelines consulted to evaluate the analytical or performance parameters *i.e. for study design, sample size, selection of data points, statistical test, number of samples etc.*	☐ No ☐ Yes If Yes, tick the applicable ☐ CLIA ☐ CLSI ☐ ISO ☐ FDA ☐ Other, Pls specify

Time taken for the development of diagnostic (in years)	
How much grant (in INR) has been received till now for the diagnostic development	
How many agencies or organisation funded the Diagnostic development	

You may withhold sensitive/confidential information.

Name:…….

Designation:……

Date:……...

Signature:…….

Annexure

**Definition of TRL-scale

(Source: https://www.birac.nic.in/webcontent/birac_trl_doc5_medical_devices_and_diagnosis_12_09_2018.pdf)

5. Medical Devices and Diagnosis

Stage	Technology Readiness Level	Definition (Medical Devices including diagnostic devices)	Definition (In vitro Diagnostic Kits & reagents)	Definition (Biomedical implants)
Ideation	TRL-1	Need identified, Basic principles observed and reported (Scientific research begins which can be translated into applied research and development)	Need identified, Basic principles observed and reported (Scientific research begins which can be translated into applied research and development)	Need identified, Basic principles observed and reported (Scientific research begins which can be translated into applied research and development)
Proof of Principle	TRL-2	Market surveillance data and competitor analysis available to support the idea. Basic device design ready and product specifications defined based on the competitor analysis and patent landscaping. FTO ensured. Development of individual components initiated.	Hypothesis formulated and protocols developed. Market surveillance data and competitor analysis available to support idea. Individual core components of kit/reagents(Antibodies/ Antigens/Aptamers/Nano particles) finalized, developed/procured for testing	Market surveillance data and competitor analysis available to support the idea. Basic implant design ready, candidate materials shortlisted and product specifications defined based on the competitor analysis and patent landscaping. FTO ensured
Proof of Concept demonstrated	TRL-3	Individual modules/Components/PCBs/Software s/Systems developed and tested separately for its functionality on a breadboard/laboratory level. Material safety, electrical safety & biocompatibility of the systems demonstrated	Individual core components optimized at lab scale. Demonstrated the limit of detection/Sensitivity with metabolite serial dilution or ELISA or spiked biological sample studies.	Material research completed and material properties of the finalized material/composites compared against benchmarks. Relevant ASTM standard tests (strength, ductility, corrosion, surface properties, antimicrobial activity, usability, shelf life etc.) on the material performed successfully. Material sterilization method finalized. Biocompatibility (ISO 10993) proven in *in vitro* cytotoxicity assays.
Proof of concept established	TRL-4	Functional Prototype developed by integration of different modules and safety, efficacy and performance of candidate device or system demonstrated in a defined laboratory, Simulated Environment or animal model (with Institutional Animal Ethics Committee approvals)	Optimized core components integrated into the kit or platform (Microfluidics/ filter paper/ LFA etc) along with the reagents to come up with a functional prototype of the kit. Integrated system tested in house with metabolite serial dilution or ELISA or spiked biological sample studies.	Material safety and or imaging compatibility proven in *in vivo* small animal model study (with Institutional Animal Ethics Committee approvals). Functional Prototype implant device developed as per the design in a near GMP condition. Sterilization and packaging established.

Early stage validation	TRL-5	Relevant IEC & ISO tests (Electromagenetic interference, Electromagnetic compatibility, Electrical safety, Biocompatibility, software test, radiation safety test drop test, packaging test, transportation test, physico – chemical and mechanical testing etc.) of the device performed and safety proven. Quality management certification (ISO13485) in place. Design iterated prototype ready to go for clinical validation. Clinical study plan approved by Institutional Ethical Committee and/or CDSCO	Integrated system tested in-house extensively with clinical samples (Blood, Urine, Sputum etc.) before taking it for clinical validation. Analytical validation of the kit completed. Shelf life, stability data of the kit reagents available. Quality management certification (ISO13485) in place Clinical study plan approved by Institutional Ethical Committee and/or CDSCO	*In vivo* pre-clinical studies performed (with Institutional Animal Ethics Committee approvals) using functional prototype implant device on the relevant small or big animal (disease) models to establish its safety (tissue reactivity/ allergy/degradability, Histopathology) and efficacy (. Quality management certification (ISO13485) in place. Design iterated prototype ready to go for clinical validation. Clinical study plan approved by Institutional Ethical Committee and/or CDSCO
	TRL-6	Fully functional clinical grade device ready with regulatory dossier for use on human subjects/patients. Quality assurance certification (like CE) applied. Pilot clinical study/trials on limited number of subjects/patients to prove safety and substantial equivalence/efficacy. Data submitted to CDSCO for Pivotal study approval	Clinical study performed on statistically significant number of samples at one or two centres to define the specificity and sensitivity of the Assay/kit. Quality assurance certification for the product applied/obtained	Clinical level implant device fabricated using clinical grade material in GMP facility with safety dossier for use on human subjects/patients. .Quality assurance certification (like CE) applied. Pilot clinical trials performed on statistically significant number of patients against the predicate implant device to prove safety, substantial equivalence/efficacy. Data submitted to CDSCO for Pivotal study approval.
Late stage Validation	TRL-7	Manufacturing lines established. Design for manufacture (DFM) finalised and devices manufactured. Documentation on design history file (DHF) ready. Pivotal clinical study/trials completed and clinical performance data submitted to CDSCO for manufacturing license	Multi-Centric Trials completed at NABL accredited centres and performance evaluation report submitted to CDSCO for Commercial license. Performance evaluation report of notified products (IVD for HIV, HCV, HBV and Blood grouping sera) obtained from NIB, Noida.	Manufacturing lines established. Design for manufacture (DFM) finalised and devices manufactured. Documentation on design history file (DHF) ready. Pivotal clinical study/trials completed and clinical performance data submitted to CDSCO for manufacturing license
Pre-commercialization	TRL-8	Manufacturing license obtained from CDSCO and commercial batch manufacturing initiated	Manufacturing license obtained and commercial scale manufacturing set up/Packing/labelling etc. Commercial batch manufacturing initiated	Manufacturing license obtained from CDSCO and commercial batch manufacturing initiated
Commercialization and post market studies	TRL-9	Commercial launch of the new device, Post marketing studies and surveillance	Commercial launch of in vitro diagnostic kit or reagents and Post marketing studies and surveillance	Commercial launch of the implant, Post marketing studies and surveillance