CamCovDx Research Team – Written evidence (COV0045)

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As part of the ERC-funded CANCERSCREEN project, we have mapped the global molecular diagnostics industry and the changing regulatory landscape. Our industry database comprises over 800 firms primarily in N America, Europe and Asia Pacific. We have data on the size, location, ownership and clinical/technological focus of firms. For the purposes of our database, we define molecular diagnostics as tests that use DNA or RNA as the analyte.

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Scope of evidence provided

We report rapid findings from an exploratory survey of the molecular diagnostics industry's response to the COVID-19 pandemic. Leveraging the CANCERSCREEN database we have gathered data on over 391 molecular diagnostics firms that are producing/developing tests for COVID-19. This is a fast-moving field and data collection remains a work-in-progress. The current analysis was generated in early April and we will share new data when it becomes available in the next fortnight.

The focus of our research coincides with the call for evidence in one area "Diagnostic tests for the virus, including PCR (nucleic acid) tests and antibody tests: their accuracy, reliability, supply and distribution."

1 Introduction

1.1 The COVID-19 testing strategies adopted by different countries are now under intense public scrutiny. National governments in countries including the USA and the UK have been criticised for failing to ramp up capacity and their performance is compared to that of states where testing rates are far higher, notably Germany and South Korea. Capacity for diagnostic testing is one of the key issues now facing policymakers. Facilitating rapid innovation and scaling up of capacity has to be balanced against the need for robust regulatory frameworks that can assure the quality of tests. Here we present data on

- 1.1.1 how the molecular diagnostics industry is responding to the COVID-19 pandemic, providing a comparative analysis of developments across the globe;
- 1.1.2 how the weakness of the current EU regulatory system raises concerns about the quality of tests

2 Background on the molecular diagnostics industry

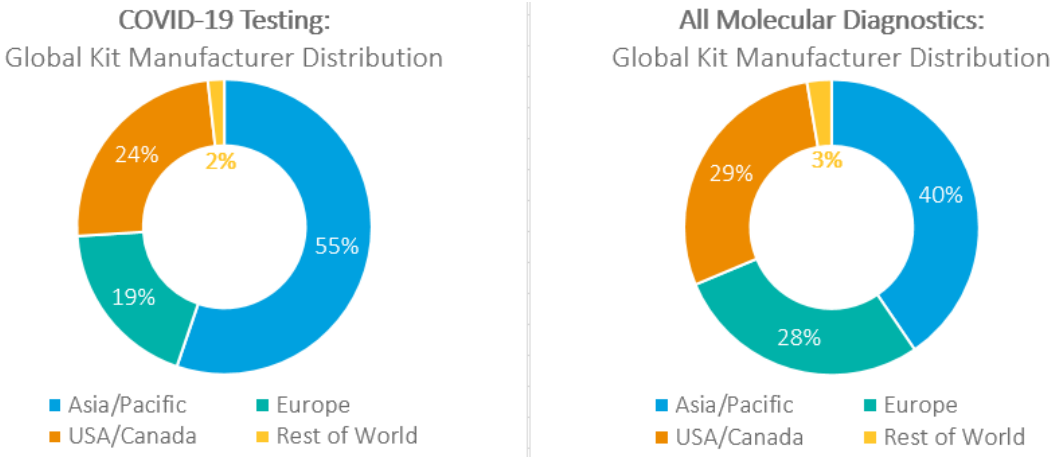
2.1 For the purposes of our research, we define molecular diagnostics as tests that use DNA or RNA as the analyte. The molecular diagnostics industry has grown rapidly since the 1980s, and is generally reported to be the fastest growing sector of the in vitro diagnostics industry. The global molecular diagnostics industry has three main clinical markets: genetic disease, cancer and

infectious disease. Many firms serve all three markets. Infectious disease is the single biggest market, for instance in Europe it generates about 60% of firm revenues.

2.2 Molecular diagnostics are based on an increasingly sophisticated range of analytic technologies including in situ hybridization (ISH), microarrays, next generation sequencing (NGS) and polymerase chain reaction (PCR). Across detection methods, there is a common trajectory towards greater automation, faster turnaround times, and from single marker testing to multiplex testing (i.e. the simultaneous detection of multiple markers). PCR is the dominant technology in infectious disease testing (whereas NGS is increasingly the technology of choice in clinical genetics and cancer). Traditionally, molecular testing has been a complex and lengthy procedure requiring considerable expertise, but a growing number of automated "sample to result" PCR systems are available that simplify and speed-up the testing process. Until recently such systems have been too large and expensive for point-of-care (POC) use in physicians' offices, but a new generation of cheaper, rapid POC molecular testing platforms are now on the market.

2.3 Comparing the global universe of molecular diagnostic kit manufacturers with the COVID-19 sub-sector, we see that Asia Pacific firms make up the majority of firms in both datasets, but their dominance is greater in the COVID-19 market. How to explain this difference? Some of it may relate to regulatory issues, and some of it may be to do with key AP markets being impacted by COVID-19 earlier, so firms needed to react faster. Some of it may be to do with state-preparedness e.g. South Korea has a large number of molecular diagnostics firms and had a national plan for pandemic preparedness.

Figure one Global distribution of molecular diagnostics kit manufacturers



2.4 In figure two we focus on the countries with the highest number of COVID-19 firms to look at the relationship between the total number of firms either marketing or developing a COVID-19 test and those firms with a test on the market. In some countries where the state has implemented large-scale testing, a higher percentage of firms have tests on the market (South Korea and Germany exemplify this). Countries like the USA and UK that are laggards in testing, have a greater gap between firms marketing tests, and firms that have said they are developing a test. This suggests that in some cases state

leadership may play an important role in influencing domestic firm behaviour. Many commentators have discussed the level of preparedness in South Korea and the rapid implementation of large-scale testing. One dimension of this which is seldom discussed is the strong relationship between the state and the manufacturing sector in South Korea. The country exemplifies what many academics term the Asian Developmental State model - a pattern of industrialisation in which the state directs economic development.

2.5 Figure three looks at the same issue from an alternate view breaking the difference down by region, suggesting that the gaps can in part also be explained by the timing of the global spread of COVID-19. If there is indeed a lag between disease outbreak in a region and industry response, then the need for state leadership to facilitate an industry response is even clearer.

Figure two Firms and tests by country of firm – comparative data on tests which are commercialised and tests which are in development

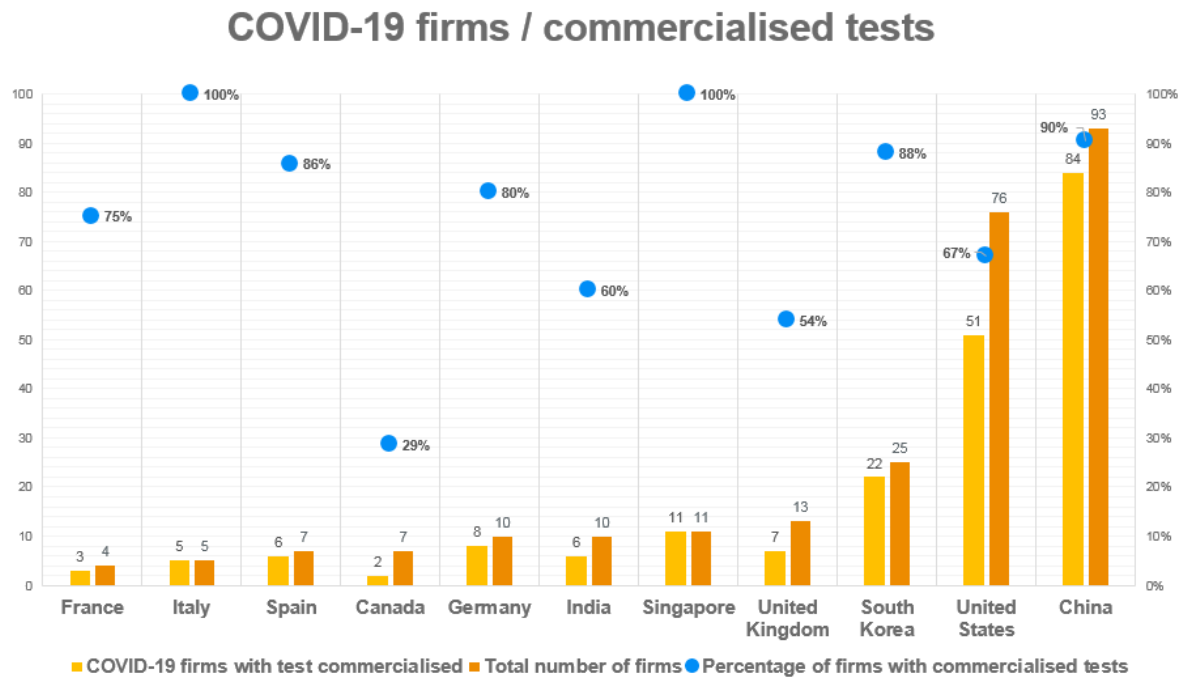
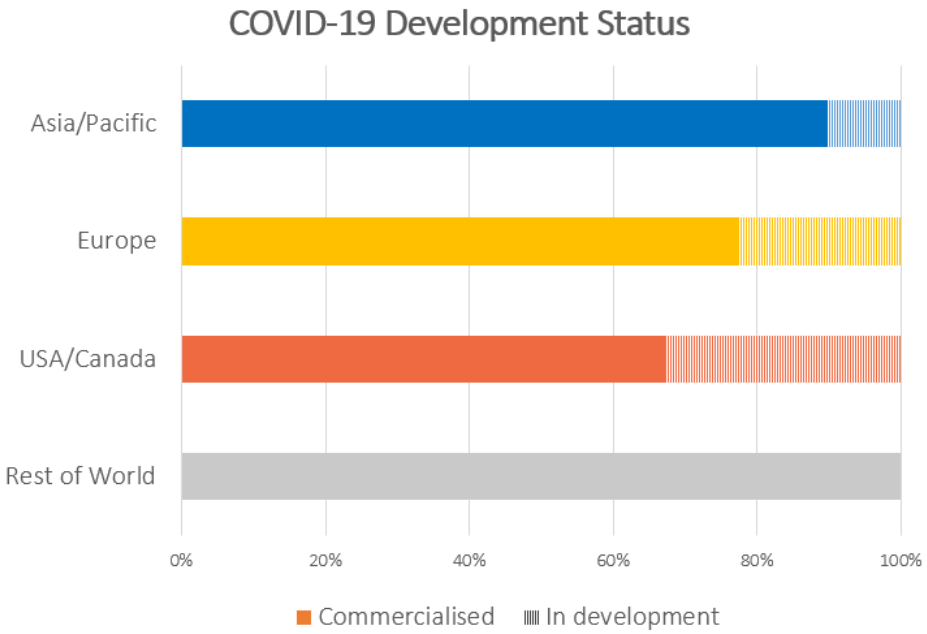


Figure three Test development status by region



3 Regulation of tests in comparative perspective

3.1 We now turn to the regulatory situation. Here we compare regulatory approvals across countries. Again, we must caution that the data was generated on 12 April and this is a rapidly-changing landscape. Many countries have implemented emergency approval/authorisation processes to accelerate market access for new COVID-19 tests: Emergency Approval (EA) or, in USA, Emergency User Authorisation (EUA). Manufacturers can also commercialise their tests as Research Use Only products. In theory RUO products are for biomedical research, not clinical testing, but in practice labs may buy RUO products and perform their own validation of the test.

3.2 In figure four we provide a breakdown of regulatory approvals by country (or in case of EU, region). The rows are approvals in each jurisdiction, the columns are location of the firm. Countries / regions differ significantly in the degree to which their market comprises foreign firms. In the EU the vast majority of firms with CE-marked tests are not EU-based: 62 firms across China, USA, South Korea and Singapore are exporting CE-marked COVID-19 tests to the EU.

Figure four Regulatory approvals by country

Regulatory Approval – Country (partial data, not all countries)

Firm location	China	USA	South Korea	Singapore	Germany	UK	Spain	India	Italy	Malaysia	France	Japan
Total # Firms	84	51	22	11	8	7	6	6	5	3	3	3
Research Use Only	29	11	4	4	2	2	1	3		2		1
EU Approval	37	11	13	1	3	5	5		4		3	
US EUA	3	30			1	1					1	
CAN Approval		7										
China Approval	24	1	1		1	1						
S. Korea Approval			7									
Australia Approval	2	5					1					
Philippines Approval	5	4	2	2	1		1					
Singapore Approval	1	3		7								
Saudi Arabia Approval		1	1		2	1						

3.3 It is striking how the EU market is highly penetrated by non-EU firms. In China, USA and South Korea the position is reversed - most firms with approved tests are domestic. There are 50% more Chinese firms with CE-mark for EU market than have approval in China. This is replicated with South Korean firms/South Korean regulatory approval. Conversely, only South Korean firms have approval in South Korea, and very few firms that are not Chinese have approval in China. Nearly all the firms with FDA EUA for the USA are US firms. Only US firms have approval in Canada (except one Swiss firm, not displayed).

3.4 There are two important policy issues to consider in relation to the EU position. Firstly, with a process of manufacturer self-certification, the barrier to market entry in the EU is very low. If the EU is to avoid becoming a dumping ground for poor quality tests, then further action must be taken. That is already happening at national level, as individual member states are forced to undertake post-market evaluation to assess the quality of tests to inform their procurement decisions. The global charity FIND is acting as a hub for sharing evaluation data on tests – this is of vital importance and must be supported by all nations.

3.5 The second issue concerns the degree to which EU countries are dependent on imported tests (an unknown at this stage). In the context of normal trading conditions, with a relatively free flow of goods within the global market, such dependence would not necessarily be a cause for concern. However, in the current crisis there have repeated media reports of shortages of medical goods and bidding wars between nations for vital supplies. Moreover, China has banned exports of tests that have not been approved by its regulatory body – the impact of this barrier to export is currently unknown.

4 The regulatory weakness of EU and regulatory reform

4.1 The EU's current risk classification system is completely inadequate. Nearly all tests are classed as low risk, allowing manufacturers to self declare regulatory compliance and give the product a CE mark, which indicates conformity with EU regulations. Once fully implemented, the EU's new IVD regulation will close this regulatory loophole, placing most molecular diagnostics

in a higher risk category, meaning they have to go through premarket review by a notified body (the regulatory authority that assesses compliance with regulations). As a result, a far broader range of diagnostic tests will be subject to independent scrutiny before they can enter the EU market.

4.2 The immediate problem is that this new system is not in place. The current pandemic, which has seen a large number of new diagnostic tests entering the European market in a very short time, and high-profile instances of tests with poor performance highlights the weakness of a regulatory system based on largely post-market controls, rather than pre-market approval. A secondary problem in the UK is our post-Brexit regulatory regime. There is a danger that the government will seek to create a more permissive regulatory framework in the UK, as part of a broader shift away from EU governance frameworks.

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