Pharmaceutical manufacturers across Asia, Africa and Latin America with the technical requirements and quality standards to manufacture mRNA vaccines

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• Why focus on mRNA vaccines?

One year after multiple effective vaccines against Covid-19 were brought to market, we have failed to vaccinate the world. The distribution of vaccines remains highly unequal. In Portugal, a high-income country, 87% of the population has been fully vaccinated; in Nigeria, the largest country on the African continent, the corresponding figure is less than 2%. The stark differences in vaccination rates are due to supply inequities: 74% of all vaccines dispensed this year went to high and upper-middle-income countries, while less than 1% went to low-income countries³. An existing shortage in vaccine supply is only set to worsen with news of the Omicron variant, and the increased demand for booster shots in high-income countries⁴⁵.

We need to be making billions more doses in order to vaccinate the world. The most effective way to do so would be by diversifying and expanding the manufacture of mRNA vaccines. Unlike older (pre-2020) vaccine technologies which are cell-based, mRNA vaccines are made through biochemical rather than biological processes. This makes for a simpler system of production, and one that is more predictable and easier to transfer to other manufacturers than previous vaccine technologies⁶. An essential consequence of the simplicity is speed: it takes three to seven days to produce a batch of the active pharmaceutical ingredient for the Pfizer/BioNTech vaccine, as compared to one month for an equivalent batch of the AstraZeneca vaccine⁷.

It should be noted that cold-chain-management of the currently approved mRNA vaccines is a challenge in developing countries; however, developers are already exploring more thermostable formulations, and it is a matter of time before we see new mRNA vaccine formulations that only require standard refrigeration.

• Can mRNA technology diversify the existing geographical base of vaccine supply?

The goal is to make billions more doses of mRNA vaccines as quickly as possible, and this can be achieved in a few different ways. At present, the two mRNA vaccines in use, Moderna and Pfizer/BioNTech, are being manufactured by these companies and their contractors, for the most

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part, in high-income, Western countries, with the exception of one full manufacturing license that BioNtech has with Fosun, in China. We suggest that the best way to make more mRNA vaccines is to geographically diversify the manufacturing of these vaccines, a strategy that would serve us in both the short and long terms. If vaccine manufacturing could be distributed across countries, and covered all continents, that would provide security, stability and independence to large parts of the world.

In the past, this has been difficult to achieve, because of the restricted number of manufacturers with experience in older (pre-2020) vaccine technologies. For instance, if we were to tabulate existing vaccine manufacturers in Africa and Latin America who have been qualified by authorities in the United States, Europe, or the World Health Organization, we would be left to work with only 1 manufacturer in Africa, and 3 in Latin America. However, because of the unique nature of mRNA technology, and its lack of cell-based, biological components, mRNA vaccines can be produced by a far larger number of existing pharmaceutical manufacturers, even if these manufacturers have no previous experience with vaccines. This is not a theoretical assumption; it is the working model that Moderna and Pfizer/BioNtech have used to successfully partner with other contract-manufacturers in order to scale up their own production.

Recent research into requirements for mRNA vaccine manufacturing from MSF and Imperial College reveals that any pharmaceutical company currently manufacturing sterile injectables (a process that requires similar competencies and facilities to those required for making an mRNA vaccine) satisfies the minimum criterion to manufacture an mRNA vaccine. Applying this criterion, and adding in a stringent quality filter, returns at least 8 sites in Africa and 6 sites in Latin America that can make mRNA vaccines, as opposed to 1 and 3 sites respectively for older vaccine technologies. In short, choosing mRNA technology for vaccines resulted in a more than threefold increase of the potential vaccine supply base.

It is important to note that this list represents a baseline scan. Our focus here is on technical feasibility. The companies identified by us will need to conduct their own ‘gap’ analysis before venturing into mRNA technology. Not every company in this list of 120 might necessarily want to start making mRNA vaccines: there are multiple factors to take into account, such as the ability to access the required investment, the strength of the drug regulatory authority in the country of manufacture, and, finally, the prospect of a strong business case.

The logic underlying this list, however, is compelling: if a company in Spain such as Rovi, that produces sterile injectables, with no experience making either biologic drugs or vaccines, can make Moderna’s vaccine, then there is no reason why a company with a similar profile based in Morocco, South Africa, Brazil, India or Bangladesh, cannot do the same – should it receive a full technology transfer from Moderna, as Rovi did.

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8 Fill-and-finish deals are excluded here as they do not involve manufacturing the actual vaccine substance.


10 WHO, Pre-Qualified Vaccines, World Health Organization <https://extranet.who.int/pqweb/vaccines/prequalified-vaccines>


Why is the Omicron variant a reason to increase mRNA vaccine manufacturing?

Scientists across the world are currently working to identify how much of a danger the Omicron variant poses, and whether the current crop of Covid-19 vaccines work against it. Regardless of the eventual findings, the emergence of this new variant means that vaccinations will increase everywhere in order to protect people, as well as to curb the amount of virus in circulation, so that the chances of new mutations and variants emerging are reduced.

In the next few years, therefore, the world will need even more vaccines than we anticipated at the beginning of 2021. In high-income countries, the emergence of the Omicron variant has already resulted in a general expansion of recommendations for booster shots; in low-income countries, the emergence of this variant has resulted in a renewed urgency for any vaccines at all.

In this regard, mRNA technology offers some distinct advantages. First, we know that the two existing mRNA vaccines – Moderna and Pfizer/BioNTech – work against the variants we have witnessed before Omicron. Second, mRNA vaccines are much easier to adapt and reformulate; earlier in the year, it took Moderna 30 days to develop a version of its vaccine for trials against a new variant, whereas, by contrast, the shortest time taken to adapt an adenoviral vaccine (such as AstraZeneca or Johnson & Johnson) has been five months. Third, the mRNA platform has significant future potential for use against other diseases, which provides private and state actors a useful long-term incentive for investing in mRNA technology today.

How did we arrive at a list of at least 120 manufacturers with the technical requirements and quality standards to make an mRNA vaccine across Asia, Africa and Latin America?

The methodology used to create this list is based on findings from recent research into mRNA vaccine manufacturing from MSF and Imperial College, to which we added additional steps with respect to geographical interest and quality assessment.

- The first step was to identify the geographical scope of the exercise, which we fixed at countries in Asia, Africa and Latin America, representing the developing world.
- The second step was to identify companies within this geographical scope who both manufactured sterile injectables and had been certified by a reputable agency or organization for good manufacturing practices (GMP) as a guarantee of adhering to the highest international quality standards.

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• In the first leg of this phase, we consulted the largest identifiable source of the cross-sectional data we were looking for (sterile injectables + certified quality) which was the European Medicines Agency’s EudraGMDP database\(^21\), where we found companies who had passed inspection of their facilities for export of a sterile pharmaceutical product to the European Union. This gave us the bulk (82%) of the companies on our list.

• In the second leg of this phase, we consulted the WHO’s Pre-Qualification project for vaccines\(^22\), as well as for biotherapeutics\(^23\), from which we added companies on the basis of WHO approval, which is a similar standard to the EU. (All vaccines and biotherapeutics are sterile injectables, whereas the reverse is not true). The WHO search gave us 15% of the companies on our list.

• In the third leg of this phase, we searched for anecdotal instances of US Food and Drug Administration approval of sterile injectables for export to the US, which involves GMP assessment of a similar standard to the EU and WHO. The US FDA database does not list records in the detail we require (it does not distinguish between approvals for pharmaceuticals in general and sterile injectables) and as a result, we relied on a selected list of companies who self-reported US FDA approvals, which we verified with media reports. This gave us the remainder (3%) of the companies on our list.

Once a draft was drawn up, we accounted for multiple facility listings of the same company, as well as mergers and acquisitions, to the extent possible\(^24\). Companies with multiple qualified facilities have been summarized under one listing, and in other cases, companies wholly or partially acquired by others are listed separately, unless fully merged.

We let a small number of subsidiaries of Western pharmaceutical companies stay on our list since they qualify under the criteria here, even though they do not have the same flexibility or independence to venture into mRNA technology as their more locally-owned counterparts. (A total of 8 companies\(^25\) in all, or 6% of the total, belong to this category; 3 in India and 5 in China).

• **A sample analysis of mRNA manufacturing potential across selected manufacturers**

In addition to identifying 120 companies with the technical requirements and quality standards to make mRNA vaccines, we spoke to a sample of these companies across Asia and Africa to understand their ability in more detail. The questions we asked of them, which they answered in the affirmative, were details of mRNA production, such as whether they had evaluated what they would need in terms of human resources and equipment, whether they had enough specialized space within their facilities or could build it quickly, and if they had access to the finances required to invest in the process.

Among the companies we spoke to are Sothema, Biocon and Beximco Pharma.

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22 WHO, Pre-Qualified Vaccines, World Health Organization <https://extranet.who.int/pqweb/vaccines/prequalified-vaccines>
24 The raw data, including a full list of facilities with the requisite quality assessments (which is a more comprehensive account than the list of companies) is available on request from the authors.
A brief profile of each of these companies follows.

**Sothema** is a publicly-listed Moroccan pharmaceutical corporation in operation since 1976\(^{26}\). The company’s annual turnover in 2019 was US$177 million. Its subsidiaries include West Afric Pharma (WAPH) in Dakar, Senegal. Sothema has traditionally made small molecules, or chemistry-based pharmaceuticals. Beginning in 2021, during the pandemic, it ventured into “fill and finish” operations for Sinopharm’s Covid-19 vaccine. In addition, the company has a 11,000 square-meter dedicated facility for sterile operations, to produce sterile injectables. It employs in the region of 10,000 people, spread across multiple production facilities. Sothema was assessed as having EU-compliant standards of GMP for the manufacture of sterile products in 2010 and 2013 (Inspecting authority: France) and in 2019 (Inspecting authority: Netherlands).

**Biocon** is a publicly-listed Indian bio-pharmaceutical manufacturer, founded in 1978\(^{27}\). In the financial year ending in March 2021, the company reported annual revenue of US$974 million. Among its subsidiaries is Syngene, a contract research-and-development organization. The company’s revenue stream primarily comes from biologic drugs, generic bio-pharmaceuticals and research services, with 81% coming in from exports and 29% from the Indian market. It employs over 13,500 people across multiple facilities. Biocon was assessed as having EU-compliant standards of GMP for the manufacture of sterile products at a facility in India in 2018 (Inspecting authority: France) and in 2020 (Inspecting authority: Ireland), as well as at a facility in Malaysia in 2019 (Inspecting authority: Ireland). The company was assessed as having WHO-compliant standards of GMP for the manufacture of an oncology biologic drug (Trastuzumab) in 2021. Additionally, the company was assessed as having United States FDA-compliant standards of GMP for the manufacture of sterile pharmaceutical products in 2017 (for Trastuzumab), in 2018 (for Pegfilgrastim) and in 2020 (for Insulin Glargine).

**Beximco Pharma** is a publicly-listed pharmaceutical company in Bangladesh that was founded in 1980\(^{28}\). In the financial year ending in 2020, the company reported annual revenue of US$345 million. Beximco has traditionally made chemistry-based small molecules, in addition to other pharmaceutical products, and is now actively exploring expansion into mRNA technology both for vaccines in the pandemic, as well as for other uses, such as oncology, in the future. The company employs in the region of 4500 people, across two plants, including its main 23-acre campus with multiple self-contained production facilities. Beximco was assessed as having EU-compliant standards of GMP for the manufacture of sterile products in 2012 and 2015 (Inspecting authority: Austria), as well as in 2019 (Inspecting authority: Germany).

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\(^{26}\) Sothema, https://sothema.com/web/

\(^{27}\) Biocon, https://www.biocon.com/

\(^{28}\) Beximco Pharma, https://beximcopharma.com/
Pharmaceutical manufacturers across Asia, Africa and Latin America with the technical requirements and quality standards to manufacture mRNA vaccines (in alphabetical order, by country)

**ASIA**

1. Abbott Healthcare
2. Accure Labs
3. Ahlcon Parenterals
4. Aspiro Pharma
5. Astral SteriTech**
6. Aurobindo Pharma
7. Bharat Biotech International
8. Biocon
9. Biological E
10. Brooks Laboratories
11. Cadila Healthcare (Zydus Cadila)*
12. Cadila Pharmaceuticals
13. Caplin Point Laboratories
14. Cipla
15. Dr Reddy’s Laboratories
16. Emcure Pharmaceuticals
17. Eugia Pharma Specialities Limited
18. Gland Pharma
19. Gufic Lifesciences
20. Haffkine Bio Pharmaceutical Corporation*
21. Hetero Labs
22. Immacule Life Sciences**
23. Indoco Remedies
24. Intas Pharmaceuticals
25. Jodas Expoim
26. Lupin
27. Maiva Pharmatech
28. Mediorals Laboratories
29. MSN Laboratories
30. Mylan Laboratories
31. Naprod Life Sciences
32. Nectar Lifesciences
33. Orchid Pharma
34. Panacea Biotech*
35. Reliance Life Sciences
36. Revacure Lifesciences
37. Sakar Healthcare
<table>
<thead>
<tr>
<th>No.</th>
<th>Company Name</th>
<th>Country</th>
</tr>
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<tbody>
<tr>
<td>38</td>
<td>Samrudh Pharmaceuticals</td>
<td>India</td>
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<tr>
<td>39</td>
<td>Sandoz</td>
<td>India</td>
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<tr>
<td>40</td>
<td>Sanofi Healthcare India*</td>
<td>India</td>
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<tr>
<td>41</td>
<td>Sanzyme</td>
<td>India</td>
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<tr>
<td>42</td>
<td>Sentiss Pharma</td>
<td>India</td>
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<td>43</td>
<td>Serum Institute of India</td>
<td>India</td>
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<td>44</td>
<td>Shilpa Medicare</td>
<td>India</td>
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<tr>
<td>45</td>
<td>Sovereign Pharma</td>
<td>India</td>
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<tr>
<td>46</td>
<td>SP Accure Labs</td>
<td>India</td>
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<td>47</td>
<td>Steril-Gene Life Sciences</td>
<td>India</td>
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<td>48</td>
<td>Strides Pharma Science</td>
<td>India</td>
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<td>49</td>
<td>Sun Pharmaceutical Industries</td>
<td>India</td>
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<td>50</td>
<td>Swiss Parenterals</td>
<td>India</td>
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<tr>
<td>51</td>
<td>USV Private Limited</td>
<td>India</td>
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<td>52</td>
<td>Venus Remedies</td>
<td>India</td>
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<td>53</td>
<td>Wintac</td>
<td>India</td>
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<td>54</td>
<td>Wockhardt**</td>
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<td>55</td>
<td>Zeiss Pharma</td>
<td>India</td>
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<td>56</td>
<td>Baxter Healthcare</td>
<td>China</td>
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<td>57</td>
<td>Beijing Institute of Biological Products*</td>
<td>China</td>
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<td>58</td>
<td>Beijing Scieecure Pharmaceutical Company</td>
<td>China</td>
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<tr>
<td>59</td>
<td>Chengdu Institute of Biological Products*</td>
<td>China</td>
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<td>60</td>
<td>Chia Tai-Tianqing Pharmaceutical Group</td>
<td>China</td>
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<td>61</td>
<td>Fresenius Kabi Pharmaceutical Company</td>
<td>China</td>
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<td>62</td>
<td>GE Healthcare</td>
<td>China</td>
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<td>63</td>
<td>Hainan Poly Pharm</td>
<td>China</td>
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<td>64</td>
<td>Hainan Shuangcheng Pharmaceuticals</td>
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<td>65</td>
<td>Hebei Dawn Pharmaceutical Co., Ltd.</td>
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<td>66</td>
<td>Hebei Huari Pharmaceuticals</td>
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<td>67</td>
<td>Hualan Biological Bacterin*</td>
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<td>68</td>
<td>Hybio Pharmaceutical Company</td>
<td>China</td>
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<td>69</td>
<td>Jiangsu Hansoh Pharmaceutical Group</td>
<td>China</td>
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<td>70</td>
<td>Jiangsu Hengrui Medicine</td>
<td>China</td>
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<tr>
<td>71</td>
<td>Lilly Suzhou Pharmaceutical Company</td>
<td>China</td>
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<tr>
<td>72</td>
<td>Linyi Dongcheng Dongyuan Biological Engineering</td>
<td>China</td>
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<td>73</td>
<td>Nanjing Kin-friend Biochemical Pharmaceutical Company</td>
<td>China</td>
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<td>74</td>
<td>NCPC Hebei Huamin Pharmaceutical Company</td>
<td>China</td>
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<td>75</td>
<td>Novo Nordisk</td>
<td>China</td>
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<td>76</td>
<td>Pfizer</td>
<td>China</td>
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<tr>
<td>77</td>
<td>Qilu Pharmaceutical Company</td>
<td>China</td>
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<td>78</td>
<td>Shandong Anxin</td>
<td>China</td>
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</table>
79 Shanghai Henlius Biopharmaceutical Company  China
80 Roche  China
81 Shenzhen China Resources Gosun Pharmaceuticals  China
82 Shenzhen Techdow Pharmaceutical Company  China
83 Shenzhen Zhijun Pharmaceutical Company  China
84 Sinopharm  China
85 Sinovac Biotech*  China
86 Wanbang Biopharmaceuticals  China
87 WuXi Biologics  China
88 Xiamen Innovax Biotech*  China
89 Zhuhai United Laboratories  China
90 Celltrion  S. Korea
91 EuBiologics*  S. Korea
92 Green Cross Corporation (GC Pharma)*  S. Korea
93 Il-Yang Pharmaceuticals*  S. Korea
94 JW Life Science  S. Korea
95 LG Life Sciences  S. Korea
96 Samsung Biologics  S. Korea
97 SK Bioscience  S. Korea
98 Taeguek Pharmaceutical Company  S. Korea
99 Imexpharm Corporation  Vietnam
100 Medochemie (Fast East)  Vietnam
101 Tenamyd Pharma  Vietnam
102 Pharmaniaga Lifescience  Malaysia
103 Xepa-Soul Pattinson  Malaysia
104 Beximco Pharmaceuticals  Bangladesh
105 GPO-MBP*  Thailand
106 PT Bio Farma*  Indonesia

AFRICA

107 Egyptian International Pharmaceutical Industries  Egypt
108 EVA Pharma  Egypt
109 Global Pharmaceutical Industries  Egypt
110 Laboratoires UNIMED  Tunisia
111 Les Laboratoires MédiS  Tunisia
112 Sothema  
113 Institut Pasteur de Dakar*  
114 Aspen Pharmacare**  

**LATIN AMERICA**

115 Antibióticos do Brasil  
116 Bio-Manguinhos/ Fiocruz*  
117 Instituto Butantan*  
118 Eriochem S.A.  
119 Synthon Chile  
120 Centro de Ingeniería Genética y Biotecnología*

Sources:

Europe: 98 out of the 120 manufacturers on this list (unmarked) exported a sterile pharmaceutical product to the European Union, and thereby had GMP certified by the European Medicines Agency. These records are listed on the EudraGMDP database; and publicly available here: (http://eudragmdp.ema.europa.eu/inspections/gmpc/searchGMPCompliance.do)

WHO: 18 of the 120 manufacturers here (marked with one *) appear on the World Health Organization’s Pre-Qualification database for vaccines, a process that includes GMP evaluation, and is publicly available here: (https://extranet.who.int/pqweb/vaccines/prequalified-vaccines). While our methodology included searching through the WHO’s Pre-Qualification database for biotherapeutics, there were no new companies to add from that list.

United States: 4 of the 120 manufacturers here (marked with two **) exported a sterile pharmaceutical product to the United States, and thereby had GMP certified by the US Food and Drug Administration. These records, while available on the US FDA database, do not list the level of pharmaceutical product detail we need, and are instead taken from individual public records on the companies’ own websites and confirmed by media reports.

Note: As a result of the methodology employed, some manufacturers have multiple successful quality assessments (from Europe, the WHO and/or the United States) but are reported here according to the first certification that is publicly available in the order listed above. For example, Biocon has received European, WHO and US approval for sterile pharmaceutical products, but is listed here as European-approved, based on the order of this list.

For the methodology behind this list, see previous pages in this document.