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European Federation of Pharmaceutical Industries and Associations

Vaccines Europe
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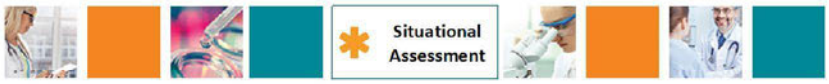
Draft ☐ Final ✱

Potential impact of coronavirus (COVID-19) on the availability of medicinal products in Europe



BLACK = updates to 29 April 2020
RED = updates to 05 April 2020

Overall assessment

As of 17 April 2020, EFPIA members report shortages to EMA and national authorities via the I-SPOC system. Overall, the situation is starting to stabilize. However, supply and manufacturing remain under pressure and while manufacturers are doing everything they can to ensure security of supply, we need the cooperation and support from European and national authorities to be able to ensure continuity of supply.

Within the European Union the situation is currently highly dynamic and everything will depend on the length of the current crisis as well as the overall level of cooperation and coordination among Member States.

We greatly appreciate the guidance from European Commission (DG SANTE) on the optimisation of supply of medicines for COVID-19. We consider that it touches upon all the major areas of concern which we have highlighted over the last weeks. We sincerely hope the guidance will be implemented in Member States, if not to the letter, at least in its intended spirit, to its full extent. Export restrictions remain in place in Belgium and have just been extended until 1st June. The threat of the restrictions causes significant uncertainty with regard to supply chain operations in the near term. While we remain hopeful that the decline in COVID-19 cases will continue in the EU, third countries that rely on supply from within the EU are increasingly being by COVID-19, and we cannot rule out further waves of COVID-19 infections within the EU. We urge the Commission to continue to work towards discontinuation of the restrictions introduced by the Belgian government and other such measures, aiming for a collaborative approach on solutions. While Hungary is manageable (companies are changing/diverting supply routes to avoid the country) it remains undesirable and an example of uncooperative behavior. While we await the implementation of the guidance, EFPIA member companies continue to have 3 major area of concern:

1. **Transparency and predictability of demand for planning purposes** – EFPIA members continue to deal with erratic and inconsistent demand for COVID-19 treatments in most European markets. This is due, in many cases, to stockpiling measures from Member States. We need more information from Member States on the supply that is really needed to meet patients' needs to help plan accordingly. It is increasingly difficult for manufacturers to assure unplanned demand and we ask for the urgent cooperation of Member States on this.

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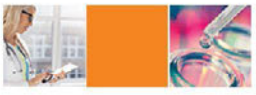
We were encouraged to hear, during the 29 April call of the Executive Steering Group on shortages of medicines caused by major events, that EMA will consider reviewing the EMA/HMAs definition of shortages as embodied in the EMA/HMA guidance of July 2019 which equates supply with demand at national level (instead of patients' needs). Such a modification is crucial if we are to ensure such a situation can be avoided in future. It is fundamentally important to look at both the supply and demand side, which is also at the heart of the Medicines for Europe/AT Kearney project supported by EFPIA and we would suggest that the demand perspective is also taken on board in the context of the I-SPOC system.

2. **Preparation for next phase (expected second wave of the pandemic)** – the industry strongly acknowledges the messages contained in the letter from Commissioner Kyriakides of 3 April to increase production of medicines as well as the intervention of Commissioner Breton on the call of 23 April asking to maintain increased production levels in preparation for a second wave. EFPIA members had started to increase production and establish increased buffer stock through their pandemic preparedness plans as of January 2020. Nonetheless, companies have 'remained in the dark' during this period (Which medicines? In what quantities? To be supplied where, and when? etc.). **We consider that we have a short window of opportunity <u>now</u> to better prepare and manage the next phase <u>collectively and in a structured way</u>. From now on and in future, we need to get the right medicines to the right hospital in the right country at the right time.** In this respect, we need the following:

   a) **reliable ECDC forecasts** on the evolution of the outbreak including how does this translate in terms of COVID-19 medication needs at country level;
   b) **transparency regarding Member States capacity and demand** – we need better information regarding Member States capacity (hospital beds capacity & availabilities, ventilation/intubation capacity; existing stockpiles accumulated during the first wave etc.). And, as mentioned above, we need a proper view of patient needs and a mechanism for better coordination of allocation of medicines across Member States.
   c) **collective dialogue with respect to which medication needs to be produced and in which quantity** – we need a better way to discuss and plan, perhaps using a mechanism similar to the I-SPOC system and rather forwards looking. Companies are becoming increasingly hesitant to continue operating and producing in the dark, concerned that supply might well exceed the demand for some medications.

3. **Regulatory flexibilities** – We appreciate the announcement of the webinar 7 May on "Q&A on Regulatory Expectations for Medicinal Products for Human Use during the COVID-19 Pandemic". To alleviate the supply situation for needed Medicinal products during the COVID lock down (even if not directly used for COVID patients), we believe that the scope of the EMA Q&A should be expanded. Furthermore, as mentioned last week, a discussion on the QP/RP discretion is needed in order to address the potential for emergency/temporary plans to maintain manufacturing and distribution operations.
   In addition, we identified the need to address the impact on regulatory commitments, such as ongoing Clinical trials that are highly impacted by the COVID-19 situation and where start and completion dates for studies are compromised. This concerns commitments under the Paediatric Regulation as well as commitments in marketing authorizations. We outline a more detailed proposal in this respect, in the main text of this document.



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The EFPIA Secretariat monitors the situation closely with members and will report back any new developments, affecting industry overall, as they arise. **In the meantime, individual companies will report their specific, detailed situation via the I-SPOC system.** We believe it would still be of great use to **establish some principles of confidentiality together with EMA for the data submitted via the I-SPOC.** At the same time, it is not obvious for our members how the country SPOCs will be handling the data submitted via the I-SPOC as well as how (or if) the data will be shared across other markets.

Continuity of manufacturing and supply is industry's priority n.1

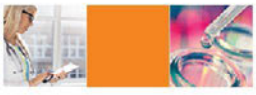
Since the start of the dialogue between EFPIA and the 3 Commissioners, we have worked on a number of challenges and threats to the continuity of manufacturing and supply of medicines in Europe. As the situation continues to be highly dynamic, this situational assessment aims to prioritize ongoing challenges (section A) but also to keep track of challenges which have been mostly resolved but where localized threats remain (section B). We have also included an indication of priority levels EFPIA considers additional action remains to be taken to fully revolve the situation.

A) ONGOING CHALLENGES:

Operational

1. **National export bans - Priority for continued action: Very High**
   Despite the concrete action taken by the European Commission and the clear improvement after the early weeks of the crisis, we continue to observe various forms/degrees of export bans. **Export restrictions remain in place in Hungary (export ban on products containing Propofol), Belgium has quarantined a number of products on the Belgium territory (Plaquenil, chloroquinin phosphas and Kaletra). Moreover, Belgian authorities impose among other obligations a mandatory notification of exports of a list of products considered essential, that has to occur 3 days prior to the shipment for exports outside the EEA, leaving the opportunity for Belgian authorities to ban the export. Belgium has prolonged these measures until 1 June. This seriously hampers our member companies' capacity to run normal supply operations, particularly owing to the fact that a number of them have either large manufacturing capacity and regional or global distribution centers in this country.**

   HUNGARY - Export restrictions remain in place in Hungary:
   - **On 9 April the Export ban covering products containing Propofol was expanded to include further molecules that are or may be used to treat COVID19 patients, including several antibiotics, analgesics and sedatives.**
   - **Hydroxychloroquine, previously banned from export, is however no longer part of the scope of export bans and can therefore now be freely exported.**
   - **Exports of all other pharma products not covered by the export ban nonetheless require demonstration that they are out of the scope via a declaration of exemption, which constitutes a significant burden. (trucks were being stopped as of 6 April).**
   - **The Government Action Group issued guidance on protecting vital services and operations, including pharmaceutical companies, putting 140 companies under the direct supervision of the Ministry of Defense. We do not know what this means in terms of future actions.**



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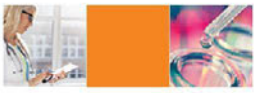
Companies have started to change/divert supply routes to avoid Hungary altogether but this remains undesirable and is example of uncooperative behavior.

FRANCE - A decree was published on March 26 at the Official Journal prohibiting the export of "specialties containing the combination lopinavir / ritonavir or hydroxychloroquine" (in other words: **export ban for 3 molecules). These are the only export bans being applied in France to date.**
With respect to muscles relaxants & anesthetics, the full stocks planned for the French market of Midazolam, Propofol, Atracurium, Cisatracurium and Rocuronium are being purchased by the State, which then distributes stocks among healthcare establishments. For these five molecules, there is no longer any passage through the usual wholesale distribution and no more direct sales from manufacturers to hospitals. There are no strictly speaking export bans applying to Midazolam, Propofol, Atracurium, Cisatracurium and Rocuronium but stock management by the French Public Health Authority to prevent the risk of tension.
The so called "Décret Ruptures/Shortages Decree" (which is about 3 years old, so not linked with COVID-19) provides that, as soon as the Medicines Agency (ANSM) publishes a list of products considered to be 'under tension of supply', wholesalers are not allowed to distribute them under parallel trade (in other words products destined by manufacturers for the French market must remain on the French market and cannot be parallel exported anymore). **Normal export business is not impacted.** The French parallel export ban covers all molecules used in the treatment of Covid19 (including molecules used for research).

Impact on supply of medicines in Africa – European Member States national export bans also have effects on supply outside of Europe. For example, several pharmaceutical manufacturers supply Western and Southern African markets from their hubs/warehouses in Belgium or Hungary.

2. **Demand planning/forecasting – Priority for continued action: Very High**
In order for EFPIA members to better plan their manufacturing capacity and make sure that all possible measures have been taken to assure continuity, **we urgently call upon Member States and the European Center for Disease Control to regularly share with us their most pessimistic predictions for the number of COVID-19 infections as well as any relevant type of sub-analysis (per age group, expected severity, per country etc.). Furthermore, any other predictions for the number of other patients whose treatment will be disrupted due to the prioritization within hospitals are welcome. This information is crucially needed by manufacturers so that they can adequately forecast demand and make the necessary planning both in terms of EU wide manufacturing capacity but also detailed distribution arrangements to supply those medicines to the right regions at the right time.** Meanwhile, EFPIA members examine a modelling exercise conducted by the Institute for Health Metrics and Evaluation (IHME) as provided by DG SANTE on 12 April. **We would like to reiterate our urgent plea to ECDC for forecasting data (any forecasting data is better than none). EFPIA members will consider all assumptions integrated by ECDC in the model they supply. We are aware that demand forecasting is not an exact science. Despite this, it crucial to have an EU level frame of reference so that manufactures can integrate this into their production planning. Manufacturers are more than conservative in their planning (meaning they will intentionally produce more than what the model will forecast) but they urgently need a starting base line.**



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In parallel, EFPIA has engaged at Secretariat level and has strongly recommended its members to join the project undertaken by Medicines for Europe and its members to assess the overall readiness of the pharmaceutical industry to meet increased demand for ICU medicines in Europe.

3. **National stockpiling requirements – Priority for continued action: High**
   An increasing number of countries but also wholesalers/traders, healthcare professionals and patients are requesting stockpiles, which are incommensurate with respect to expected demand following from company epidemiological estimates (especially for non COVID-19 treatments, e.g. cardio-metabolic). This continues to disrupt supply in this critical moment preventing other countries from getting access to the medicines and vaccines they need. Companies should not be forced to support any request to stockpile additional volumes within a specific country to ensure they can continue to supply against patient need, helping to ensure continuity of supply across Europe and the globe. Where companies see a real increase in demand for some products they do their utmost to continue to supply, demands for stockpiling lead to some very difficult choices to be made.

   We welcome the publication of the Guidelines on the optimal and rational supply of medicines to avoid shortages during the COVID-19 outbreak on 8 April and we ask that the European Commission clearly act upon those countries introducing unilateral stockpiling requirements that put at risk the overall supply of critical COVID-19 medicines in Europe.

4. **Increased demand for some product categories and threats of unilateral decisions by Member States – Priority for continued action: Medium**
   For some categories of products (e.g. HIV, pneumococcal vaccines) that can be used in the treatment of COVID-19 some companies are currently facing an evolving unstable situation, with significant increased demand from all countries for some of their HIV products (stockpiling), the need to guarantee needs for HIV patients, the threat of seizure of pharmaceutical supplies or stocks in several countries via emergency power, etc. Vaccine manufacturers observe an increased demand for some vaccines for respiratory diseases, e.g., pneumococcal, pertussis and influenza vaccines and manufacturers are currently reviewing whether current production capabilities can be increased. **The increase in demand for pneumococcal vaccines over the last few weeks in certain markets, manufacturers are experiencing intermittent backorders. This increase has just occurred, so manufacturers are evaluating the pattern of demand to determine the duration of the stockout and have adjusted production schedules to replenish as soon as possible.**

5. **Lack of coordination in treatment protocol for COVID-19 potential treatment candidates – Priority for continued action: Medium**
   One additional challenge, closely related to the stockpiling requirements relates to how the various potential treatments for COVID-19 are used off-label. EFPIA members observe inconsistent treatment protocols between countries but also within countries which leads to erratic use of medicines. Different treatment protocols also lead to complicated dose allocation further exacerbated by different pack sizes in different member states. Moreover, when companies are asked about treatment protocols they are unable to provide such information as, from a regulatory and legal point of view, these treatments are still experimental. **We ask the EMA to work with national regulatory agencies and to issue streamlined treatment guidelines for all Member States.**

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Research continuity

EFPIA is concerned with the interruption or disruption of numerous R&D projects, and welcomes in this regard the upcoming guidance of the European Commission on the continuation of clinical trials. **It is becoming crucial that alignment of practices actually happens across Member States. Numerous cross-country clinical trials are at risk of delays or, worse, of their results being subject to bias or inconclusive due to variations in how patients have been treated or followed-up.**

1. **Clinical trials continuity** - COVID-19 is materially impacting global medicines development programmes (clinical trials, regulatory approval delays, inspections, etc.). Europe hosts **one third (4,436)** of the world's 13,490 ongoing clinical trials[1] across all phases. Patients involved in these trials, evaluating 1988 candidate treatments including 750 for rare diseases[2], depend on us to work together to retain the value of this collective investment during this time of crisis. In the case of clinical trials, challenges have been experienced due to quarantines, site closures, travel limitations, disruptions in supply chain for investigational and ancillary products and infection of trial investigators and patients. All of these challenges may lead to discontinuities in the protocol management and data integrity of trials, which threatens to devalue the considerable investment by patients, investigators, healthcare organisations and sponsors.

2. **Maintaining clinical research in Europe requires clear guidance and flexibility under these challenging circumstances.** Even where infection hasn't directly intervened, quarantine, social distancing and broader COVID-19 concerns may prevent patients from being able to reach the trial site. Organisations managing and sponsoring clinical trials are also experiencing a higher proportion of staff working from home during this period. Monitoring, data collection, investigational products supply and lab and imaging work may be affected. This is leading to reports of protocol and standard operating procedure deviations due to missed visits, or changes in processes. Flexible approaches (e.g. remote monitoring, homecare visits, direct shipment of drug) that maintain the standards of GCP but with managed alternatives to ensure trial integrity and patient benefit are urgently needed.

   Conduct of vaccine clinical trials – vaccine manufacturers have put on-hold or are adapting the design of ongoing trials impacted by COVID-19 measures. In order to ensure the continuum of development plans, we need **EMA/HMA to allow a rapid restart of studies put on hold after the crisis, as well as expedited review of amendments of impacted trials.** In addition, timelines for evaluation of new Clinical Trials Applications (CTAs) should follow the normal timelines as much as possible.

3. The oversight of clinical trials is done at national level which is resulting in a patchwork of solutions - a **pan-European approach (consolidated guidance, good practice sharing, points to consider) may mitigate and slow down the disruption of clinical research. International alignment** on these measures beyond Europe would also ensure that this exceptional situation is consistently addressed in the global programme of clinical research, for the reliance of all patients and healthcare systems around the world.

4. We appreciate the guidance (*March 20, rev March 27, update 28 April*) issued by EMA, the GCP Inspectors Working Group, the Clinical Trials Facilitation and Coordination (CTFG, HMA), the Clinical Trials Expert Group (CTEG) and the European Commission (EC) and the biostatistics-focused

[1] Informa CiteLine Database, as reported in the BIO/BioCentury Survey, March 2020.
[2] Ibid

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guidance issued by the EMA. The flexibilities in the former will support the continuation of clinical research in these challenging times, as far as possible. However, the guidance only reflects where concurrence could be reached, and we ask that all parties make best efforts to align across Member States and to be as pragmatic as possible.

5. We also still need National Competent Authorities (NCAs) to apply these flexibilities to the trials in their jurisdictions, and we would ask the EU authorities to proactively engage with all NCAs to achieve this in practice. Our overarching ask to the EU and Member State authorities is **to complete the task of alignment** on the necessary flexibilities for the conduct on clinical trials and the **means to address data integrity** to ensure that these European trials are not wasted opportunities to advance healthcare for the future.

6. Because of pressures on healthcare systems, companies are still temporarily halting trial recruitment and trial beginnings in many cases. Practical changes are being explored to address clinical design requirements (e.g. endpoint measurement) where in-person clinical visits are not possible. The impact of these collective changes has the potential to weigh down the European clinical research environment for many months to come, and we will continue to seek solutions with the EU and Member State authorities that are efficient (e.g. limited requirement for substantial modifications) and effective (e.g. preserving data integrity).

7. **Impact on studies that are part of regulatory commitments** - studies can be regulatory commitments in some instance, and delays will impact the ability of companies to fulfil these commitments:

   - within a paediatric investigation plan (PIP): date of start/completion of the study, date of completion of the PIP
   - within a marketing authorisation: timelines of studies (start/finish) which are part of specific obligations of conditional MAs, or imposed post-authorisation studies, timelines for the submission of protocols, interim or final study reports, compliance with Art 46 timelines.

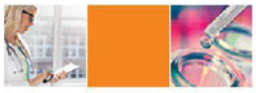
   While the Covid-19 situation is ongoing: we propose to establish a system for developers to notify EMA/NCAs proactively of commitments that are impacted by Covid-19, including why and how. Once this notification has been done, EMA/NCAs can see what is the most appropriate action to take e.g. moratorium on the completion of the commitment (e.g. 6 months by default) or instruct the developer on when and how they should re-contact the Agency to adapt their timelines, ideally with similar recommendations.

   Once the Covid-19 situation is over: we propose to allow the timelines to be adjusted retrospectively using streamlined and flexible processes to e.g. modify at a later date the timelines of PIP measures and/or PIP completion or to push forward the date of completion of a post-authorisation study.

   These measures will greatly reduce the administrative burden for both regulators and industry, while allowing visibility of the way the Covid-19 crisis is affecting commitments.

Regulatory

The updated Q&As document published on 20 April included some additional helpful guidance on manufacturing/supply GMP and GDP issues, However, industry wishes to re-emphasise the need to address the scope of regulatory flexibility and requests for QP/RP extended discretion and made in the industry paper of 6 April. Specifically:



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1. **Ensuring emergency measures are applicable to ongoing manufacturing and distribution operations for ALL medicines to avoid shortages (not just for medicinal products intended for use in COVID-19 patients)** - Given the importance of maintaining supply of all medicinal products to our patients, to avoid exacerbating co-morbidities in vulnerable patient groups or creating additional concern about the supply of medicines in the general population, we urge that suitable regulatory measures that are applicable for all medicinal products are introduced as soon as possible.
2. **Maintaining appropriate GMDP through extended QP/RP (Qualified Person, Responsible Person) discretion** - The need for personnel working in manufacturing and laboratory facilities to self-isolate in the event of suspected COVID-19 infection (even if subsequently found to be a false alarm), can rapidly lead to deviations from normal operations needed to support fulfilment of GMDP and regulatory obligations including, for example, validation and stability testing, maintenance etc.

   Such deviations need to be documented and investigated, and QPs and RPs must take these deviations into account when making decisions about release of medicinal products to the market. QPs and RPs are duly qualified to use discretion to make appropriate risk-based decisions in the current emergency on a case-by-case basis.

The below table maps out how the Q&A has responded to the original requests from the EU manufacturing and supply chain trade associations. The requests for such regulatory 'flexibility' were made without jeopardizing the quality and security of products for continuation of manufacturing and supply of products on the EU market

Original industry requests	How the EMA has integrated them
Fast track regulatory processes related to COVID 19 (variations as IA IN/ MAs). a. System of labelling the process COVID19 URGENT b. Remove the need for some conditions/documentation to be provided with some variations to allow their approval in emergency situations.	We believe the flexibility provided by the set-up of QP oversight could be further strengthened.
To ship products between countries without the need to repackage - flexibility on language/ leaflet/ packaging/ pack size	We appreciate the guidance and will ask for confirmation that the scope also applies for non COVID treatments and procedures where there is also a risk of shortage.
Fast acceptance of products with valid MA from other countries	We appreciate the guidance and will ask for confirmation that the scope also applies for non COVID treatments and procedures where there is also a risk of shortage.
Relieve on administrative burden (e.g. original copies of documents with wet signatures in submissions etc.)	We believe further progress is needed on regulatory adaptations such as: • Emphasizing the need for waiving original copies of documents with wet signatures to avoid need for face to face visits.

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	• General implementation of digital signatures instead of wet signatures • Permit the provision of user testing as a commitment within procedures. • Permit the use of electronic distribution methods for DHCPs and educational materials to effectively reach HCPs and reduce the need for manual dissemination procedures
Extend the grace period for renewals in order to free up resources for more urgent submissions.	We appreciate the guidance.
To accelerate approval for new products that are used in COVID19 treatments.	To be prepared for upcoming future filings EFPIA / Vaccines for Europe have particular interest in following up on this topic on a one to one basis with key EU Regulators.

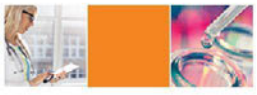
Further comments and clarifications will be shared in the regular common feedback from industry associations.

Strategic/Worldwide

1. **Proactive approach with the US - Priority for continued action: Very High**
   We should learn from recent experience and the Commission should pro-actively reach out to the US administration as several companies have major manufacturing sites located in the US supplying the entire world market. We call upon the Commission to proactively set up a sustained dialogue with the US administration in order to avoid any unilateral US decision that could negatively impact the supply of medicines to Europe. For **the research-based industry, the ability to maintain manufacturing and supply chain operations without any hinderance with the US is perhaps more important than the same with China or India.**

2. **Export bans** (India and South Africa) - **Priority for continued action: High**
   The same export restrictions which affect manufacturing and distribution within the European Union are enacted worldwide as well, especially by India. **We call upon the European Commission to address this topic at the highest diplomatic level.** Furthermore, in addition to the export restrictions, the situation is now aggravated by the restrictions of mobility of Indian workers. We urge the Commission to get support from Indian authorities to secure letters allowing manufacturing employees and suppliers to go to work. It is important to ensure labour but also transportation and customer officials are available to allow free flow of trade.

   Following increased action from Commissioner Kyriakides, the Indian Government amended their export policy on 6 April and lifted the export ban for a number of APIs & formulations that are important for the production of medicines in Europe. This is a very important first step but unfortunately some key products were included. The Indian Ministry of External Affairs initially stated that paracetamol and Hydroxychloroquine (HCQ) would be kept in a licensed category and their demand position would be continuously monitored. The Ministry stated also that in view of



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the humanitarian aspects of the pandemic, it had been decided that India would license paracetamol and HCQ in appropriate quantities to all our neighbouring countries who were dependent on India's capabilities, as well as some nations who had been particularly badly affected by the pandemic.

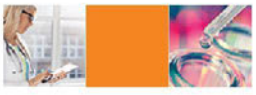
Following the measures adopted on 6 April, India announced on 16 of April that it would also allow exports of finished paracetamol products as well paracetamol API (but in a limited quantity). For these products, an application from a national government requesting an export exemption is still needed. We have been informed by Indian Pharmaceutical Trade associations that there is currently enough paracetamol API to supply the Indian population for 4-5 months so there is enough supply to cover the local market. The restrictions on APIs exports are seriously impacting European manufacturers who could run out of stocks in the next days.

South Africa has implemented a new measure requiring application for export permits for all medicines including to Europe, in the context of COVID-19. Similarly to India, this adds a lot of complexity and uncertainty to the usual process.

We propose to **use the system of I-SPOCs (as set-up with EMA)** to immediately obtain exact information from companies to obtain an overview of those registered/authorized medicinal products/raw materials (both for human and veterinary use) that could be potentially impacted by these measures. This could be done immediately at EU level and shared with national authorities.

3. **Air freight of critical medicines – Priority for continued action: High**
Pharmaceutical manufacturers rely on capacity in passenger flights to ship medicines and ingredients rapidly and securely. With the spread of the COVID-19 outbreak, we have seen a dramatic reduction in passenger flights that normally carry these pharmaceutical goods. We cannot find viable alternatives that allow manufacturers to continue the much-needed flow of goods required to maintain production of medicines for patients. Addressing this issue requires coordination between the European Commission, Governments, air carriers, logistics operators and industry to ensure that we can continue to produce and ship medicines to where they are needed. The reduction of air freight should not be considered only from the angle of Asia (India and China are major sources of manufacturing) but also from the angle of USA where several companies have major manufacturing sites supplying the entire world market. We call upon the Commission to proactively set up a sustained dialogue with the US administration in order to avoid any unilateral US decision that could negatively impact the supply of medicines to Europe.

4. **A "European strategy for essential medicines for respiratory and intensive care use". Priority for continued action: Medium**
This would entail:
    - Precise demand data gathering by country and region, precise manufacturing data and precise API availability data – by the EMA via the I-SPOC system
    - Allocation principles per country – by European Commission and Member States
    - Agreement on no hoarding / no excessive demands by member states – by Commission and Member States
    - Similarly, agreement not to control exports from e.g. manufacturing / distributor countries – by Member States
    - Build an emergency stockpile for exceptional use



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5. **World-wide acceptance of electronically signed certifications from EMA – Priority for continued action: Medium**
   On 30 March EMA announced that they will no longer provide printed certificates but only electronically signed and authenticated certificates to maintain EMA's ability to provide these documents during the COVID-19 pandemic. The printed certificate service will be resumed back once measures to reduce the spread of COVID-19 are lifted. While we very much welcome the measure and we consider it to be practical during this crisis, **we anticipate that some regulators in third countries may not be ready to accept electronic certificates. In addition, we expect that some consulates will not accept electronically signed certificates for the legalization process.** EMA have notified EFPIA that the Agency has communicated these arrangements to WHO as well as to some third countries through their network. We welcome this outreach, and we would like to ask **EMA, and National Competent Authorities, to document the efforts to communicate their certification scheme arrangements during the pandemic.** If these are documented on the EMA and NCA websites, companies can then refer regulatory authorities to the website for confirmation of process.

B) RESOLVED (Situation has strongly improved, but some localized challenges remain):

During the last few weeks, a number of initial hurdles have been largely overcome, although we continue to monitor the situation closely. These concern mainly the following areas:

1. **Dedicated 'Green-lanes' for medicines/vaccines/medical and protective equipment at borders**
2. **Manufacturing cadence – Need for pharmaceutical companies to be listed as priority/essential activities for distribution of PPE at national level**
3. **Free movement of key/critical employees in pharmaceutical manufacturing and distribution.**
4. **Supply chain disruptions that could be caused due to lack of action on the side of the local authorities to better manage the 'panic' purchase of prescription medicines at the pharmacy level**

Detailed explanation regarding the above has been provided in previous briefings.

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Appendix 1

Vaccines Europe's concerns related to the impact of the COVID-19 crisis

*** 5 May 2020 submission***

Issues related to vaccine manufacturing and supply

General statement

To this point, manufacturers have not experienced vaccine shortages but this is a dynamic situation; we continue to monitor all parts of supply chains closely and proactively assessing existing contingency plans. In addition, Companies have established appropriate incident management teams and have manufacturing continuity plans.

Increase demand for vaccines against respiratory diseases

Some VE members are currently experiencing increased demand for vaccines against respiratory diseases (influenza, pneumococcal and pertussis-containing vaccines) in some MSs such as (10)(2a)
(10)(2a)
This is the situation on 2nd of April, but other MSs may also increase their demand in the coming days/weeks. Vaccines have long cycle times of production and to match increasing vaccines needs require long-term demand anticipation. There are also regulatory barriers to move products across **borders within and from outside the EU. Manufacturers are evaluating the pattern of demand to** determine the duration of the stockout and have adjusted production schedules to replenish as soon as possible.

Vaccines Europe's call: there is a need for the Members States to urgently review the forecasts of vaccine demand and to engage with individual manufacturers to inform them on their needs regarding the vaccines against respiratory diseases and jointly find solution to remove the regulatory barriers in terms of labelling and packaging to allow movement of products within the EU and from outside the EU.

Vaccines Europe observes some flexibility from EU National Competent Authorities on labelling/packaging requirements to avoid shortages, a good example is the acceptance by German authorities of Japanese packs for Pneumovax 23, a pneumococcal vaccine (link to press release: https://www.pei.de/EN/newsroom/hp-news/2020/200401-pneumococcal-vaccines-from-japan.html)

EU seasonal flu vaccine NH market supply delivery by manufacturers usually starts from late-July each year following the WHO northern hemisphere flu vaccine strain recommendation that typically occurs by end of February. Given this tight timeline, preparation for vaccine manufacture commences 12 months earlier with sourcing of e.g. raw materials, critical reagents, disposables and "at-risk" flu vaccine strain manufacture (potentially several months earlier). The WHO recommends flu vaccine strains (n=3-4) which are developed, manufactured, formulated into tri-/quadrivalent vaccines, tested and released for supply – in collaboration with EU and member states regulatory/health agencies. Manufacturers ship released flu vaccines to the EU between late-July and mid-October for administration from September potentially up to February the following year. Availability of seasonal flu vaccine doses ultimately depends

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on an individual manufacturer's capacity. However, this 12-18-month supply lead time explains why an **unexpected, significantly increased demand for 2020-2021 seasonal flu vaccine at this point in time is hardly/not manageable by vaccine manufacturers**. Such requests need to be made as early as possible before the flu season, ideally, before manufacturers start sourcing materials, reagents and disposables i.e. 12 months before WHO recommends the northern hemisphere flu vaccine strains.

EU member states requests for marginal increases in 2020-2021 seasonal flu vaccine volumes have already been received by a number of manufacturers who are currently preparing to supply EU markets. In addition to these marginal increases already being addressed, **only limited marginal increases are likely to be accommodated now (w/c 4th May 2020).** Overall ability to meet country-specific increased demands depends on the manufacturer.

Vaccine manufacturers currently foresee to deliver their commitments to the EU for the 2020-2021 season, but manufacturers do not have enough visibility on potential further increase of demand, therefore, they are not able to answer whether there will be shortages or not for influenza 2020-2021 season.

Mechanisms for early and continuous dialogue between manufacturers and health authorities should be established to better anticipate the evolution of vaccination recommendations and more accurately forecast vaccine demand particularly if significant vaccine volumes will be required in future.

Service providers and providers of raw material

Some service providers and providers of raw material are not able to maintain their normal operations as they are not considered critical businesses by authorities in their country. This is becoming an urgent matter particularly for medicines and could also create a future health problem for vaccines due to the long leads to manufacture vaccines. It is important that not only pharmaceutical manufacturers but also service providers used by manufacturers are classified as essential service allowing for continued supply despite the "lockdown". **We urge European authorities** to provide clear guidelines to member states to ensure both manufacturers and service providers are considered essential business and can continue to operate allowing continued manufacturing and supply of key medicines and vaccines.

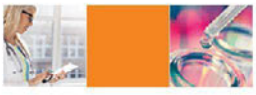
In addition, one of the concerns is that vaccines produced today may reach the market only in months/years from now.

Vaccines Europe's call: there is a need for more regulatory flexibility to ensure that measures taken by manufacturers to ensure production today during the crisis (e.g. change of raw material producers) are considered acceptable from a regulatory perspective when the vaccine lots will reach the market in the future. Regulatory flexibility is particularly important at the moment considering that both vaccine manufacturers and authorities are facing challenges due to the increase of activities in parallel with increased absenteeism and containment measures.

Disruptions in the supply/distribution chain of ingredients/semi-finished and finished products

Disruptions in the supply/distribution chain of ingredients/semi-finished and finished products within the EU have significantly decreased thanks to efforts from EC and MSs.

With regards to disruptions in supplies from outside the EU, Vaccines Europe member companies have not reported so far disruption for finished products and are still assessing the situation for raw material and



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reagents. One company reported that semi-finished goods sourced from the US packed at a French site have been significantly delayed due to flight cancellations.

Protective gear (PPE)

Vaccines Europe members are facing significant tightness of supply of PPE. Vaccines Europe members are open to look at collaborations with competent authorities to further secure priority safety equipment for employees that are critical in securing manufacturing and supply of vaccines.

One company has reported that hydroalcoholic gels and thermometers are also missing in production sites, like everywhere in community pharmacies. This company has started its own production of hydroalcoholic gel but is dependent of raw material.

Any action that could accelerate to shipment of PPE and hygiene material is welcome. Otherwise, production sites will be obliged to close if hygiene measures cannot be maintained. **We call upon Member States to ensure that pharmaceutical companies are listed on the priority list for distribution/supply of PPE at national level.**

Vaccines Europe was reported that some problems continue in the supply of protective equipment (masks and gloves) in countries such as Belgium, France, Germany and Italy.

Electronic Certificates of Pharmaceutical Products (eCPPs)

Vaccines Europe welcomes EMA publication on its website regarding eCPPs. Vaccines Europe would like to encourage all National Competent Authorities issuing CPPs to follow a similar approach.

World-wide acceptance of electronically signed certifications from EMA – On 30 March EMA announced that they will no longer provide printed certificates but only electronically signed and authenticated certificates to maintain EMA's ability to provide these documents during the COVID-19 pandemic. The printed certificate service will be resumed back once measures to reduce the spread of COVID-19 are lifted. While we very much welcome the measure and we consider it to be practical during this crisis, **we understand that some regulators in third countries are not accepting electronic certificates (** (10)(2a) **and** (10)(2a) **. In addition, we expect that some consulates will not accept electronically signed certificates for the legalization process.** EMA have notified that the Agency has communicated these arrangements to WHO as well as to some third countries through their network. We welcome this outreach, and we would like to ask **EMA and HMA (coordinating the National Competent Authorities) to document the efforts to communicate their certification scheme arrangements during the pandemic.** If these are documented on the EMA and NCA websites, companies can then refer regulatory authorities to the website for confirmation of process.
Vaccines Europe together with EFPIA is collecting information about e-CPPs and will submit the list of countries, which are not accepting eCPP by end of April/beginning of May.

Vaccines Europe welcomes the new clarification document, issued by Human Medicines Division on the 20 April 2020 (EMA/206719/2020): " Information note on the format and validity of electronic certificates for medicines issued by the European Medicines Agency" and published *on the EMA webpage*.

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Issues related to vaccine clinical trials

Vaccines Europe acknowledges the publication by EMA of the guidance on Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic but wants to reiterate that harmonised implementation of the guidance across MSs is key and should be encouraged by EMA/HMA. Version 2 of the guidance provides useful clarifications. Vaccines Europe members are still assessing whether some further adjustments/clarifications are needed and will continue to communicate with EMA on the topic as needed.

Vaccines Europe also welcomes the ICMRA report published March 24th, 2020. It is essential to set up a continuous dialogue between EMA, FDA, WHO and other relevant authorities and including vaccine manufacturers to ensure alignment between authorities on regulatory requirements to be met to obtain marketing authorisation of vaccines against COVID-19 within the shortest possible timelines.

Some vaccine manufacturers are developing vaccines against COVID-19 based on Genetically Modified Organisms (GMOs). Harmonisation of GMO applications/requirements across members states in EU is critical for an accelerated start of clinical trials. Vaccines Europe asks EMA and EC to facilitate alignment of requirements across countries as this would avoid lengthy interactions between manufacturers and relevant authorities.

Finally, vaccine manufacturers want to highlight that they have put on-hold or are adapting the design of ongoing trials impacted by COVID-19 measures. In order to ensure the continuity of development plans, Companies are expecting EMA/HMA to facilitate rapid restart of studies put on hold after the crisis, as well as expedited review of amendments of impacted trials. In addition, timelines for evaluation of new Clinical Trials Applications (CTAs) should follow the normal timelines as much as possible.

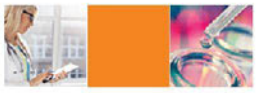
Issues related to regulatory aspects

Vaccines Europe stresses the importance of regulatory flexibility during Covid-19 crisis and is working with other associations on proposals that will be submitted to EMA.

Industry needs regulatory flexibilities, set out appropriately as guidance documents by the EU and Members State authorities, to facilitate the development and supply of all medicinal products during the COVID-19 pandemic: by having clear guidance, we can expedite action and avoid delays from regularly referring back to authorities on a case by case basis.

As per the European regulation, approval of some new vaccines is subject to site(s) inspection conduct (e.g. non-European manufacturing sites) and release of the GMP certificate. Several ongoing centralized registration procedures require manufacturing and control site's inspections to happen in a given timeframe to allow that a positive CHMP opinion be granted followed by the grant of the Marketing Authorisation (MA). Some of these inspections have already been postponed due to the COVID-19 and the subsequent inability of EU Member States' inspectors to travel to the concerned countries; should the situation last for few more months, any further delay in conduct of these inspections will put at stake the timely release of the MA.

In such particular situations and in order to avoid any delay in market introduction of new vaccines, the applicant and the manufacturing sites should closely collaborate with EMA and the designed Member



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States' inspectorates as required in order to assess GMP compliance status of the manufacturing sites. Flexibility and /or demonstration of agility would be required to temporarily mitigate sponsors' reporting potential delays. This should include the possibility of virtual inspection and/or mutual recognition of the inspections conducted by other (European or non-European) authorities. Please note that vaccines are not included in the MRA between EU and US on GMP inspections.
Paper submissions: Greece had removed the need of paper submissions but last week has re-introduced this requirement saying that it is imposed by their legal department.

Issues related to the evolution of the COVID epidemics and impact on vaccines development and manufacturing strategies

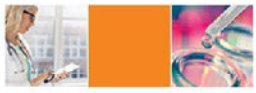
In order to adjust vaccines development and manufacturing capacity, vaccine manufacturers need to work on assumptions of the evolution of COVID-19 epidemics in Europe. Several academics and research teams are working on this and it is our understanding that ECDC is coordinating the European work to guide the Member States. Vaccine manufacturers need to get access to the modelling data as quickly as possible as the preparation of clinical trials is ongoing and building up manufacturing capacity takes time. In addition, we consider that it would be useful to establish a continuous dialogue with the ECDC as the situation is expected to significantly change over the coming months.

Vaccines Europe had a first meeting with ECDC to discuss the epidemiology modelling data and way of cooperation to design the clinical trials of Covid-19 vaccines on 21 April.

The priority now for the majority of the Vaccines Europe members is to develop or support the development and manufacturing of the COVID-19 vaccine, which is a major undertaking that will have a significant impact on the development of other new vaccines. For this, we need to work together to plan the clinical trials, identify the regulatory bottlenecks, see how the scale-up production can be supported to produce the needed vaccine doses and how the vaccines will be distributed. **Vaccines Europe calls on the Commission to address all these issues in a timely manner and in coordination between industry, Member States and EU authorities.**

Although no shortages have been reported as far as we know, the situation is not back to normal. Each company keeps the crisis management teams in place and assess on a daily basis the situation and the needs for specific actions to maintain the continuity of supply. Vaccines manufacturers are global manufacturers and Europe plays a critical role for the supply of vaccines in the non-EU countries. One of the main issues today remains air transport between Europe and the rest of the world due to the restrictions of flights.

We have seen a publication from GAVI and UNICEF mentioning that they have problems to deliver the doses to 15 African countries out of 45 and to 8 Asian countries. One manufacturer has confirmed that there is no limitation to supply and make vaccines available to UNICEF logistics providers, therefore, the most likely explanation is that UNICEF has challenges to distribute the doses to their final destinations.



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Appendix 2

Ongoing R&D programmes (up to 28 April 2020)

Treatment developments

- AbbVie announced it is partnering with global authorities to determine the effectiveness of HIV drugs in treating COVID-19. AbbVie is supporting clinical studies and basic research with lopinavir/ritonavir, working closely with European health authorities and the U.S. Food and Drug Administration (FDA), Centers for Disease Control and Prevention, National Institutes of Health and the Biomedical Advanced Research and Development Authority to coordinate these efforts.
- Amgen and Adaptive Biotechnologies (Seattle, USA) are partnering to combine expertise to discover and develop fully human neutralizing antibodies targeting SARS-CoV-2 to potentially prevent or treat COVID-19.
- AstraZeneca's Research and Development (R&D) teams have also been working expeditiously to identify monoclonal antibodies to progress towards clinical trial evaluation as a treatment to prevent COVID-19. More than 50 virology, immunology, respiratory, and protein engineering experts across research, clinical, regulatory, and manufacturing are placing the highest priority on developing a treatment to minimise the global impact of the disease.
- AstraZeneca will initiate a randomised, global clinical trial to assess the potential of Calquence (acalabrutinib) in the treatment of the exaggerated immune response (cytokine storm) associated with COVID-19 infection in severely ill patients. Calquence is approved for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) in the US and a few other countries with an active global filing programme.
- Bayer is cooperating with governments and health authorities worldwide to provide them with available stock of Bayer products that have indicated early signs of potential efficacy in treating patients with COVID-19, including Resochin® and to support clinical trials on further testing. Bayer has also joined forces with other manufacturers in the COVID-19 Therapeutics Accelerator Initiative, initiated by the Bill & Melinda Gates Foundation, thereby opening up our vast compound library to find and develop effective novel compounds against COVID-19. Bayer also responded to the European Innovation Medicine Initiative's call for the "Development of therapeutics and diagnostics combatting coronavirus infections" with an in-kind contribution covering the screening of a molecular target against the Bayer substance library.
- Boehringer Ingelheim immediately identified the areas of expertise, where we can best contribute to developing therapies for COVID-19 in close collaboration with academic researchers, international institutions and others in the pharma industry. Boehringer Ingelheim has joined a fast track call for project submissions to develop therapies and diagnostic tools initiated by the Innovative Medicines Initiative (IMI) of the European Union to accelerate the development of potential therapies for COVID-19. Boehringer Ingelheim is working to develop neutralizing antibodies against the SARS-CoV-2 spike protein. In addition, we are investigating our existing pipeline and in-market compounds as well as compounds from former HIV and HCV research activities. Furthermore, Boehringer Ingelheim is conducting a computational screening of its entire molecule library of more than one million compounds with the aim of identifying novel small molecules with activity against the virus.
- Boehringer Ingelheim is searching for novel virus-neutralizing antibodies. It is also screening its entire molecule library for compounds that could target the virus. Boehringer Ingelheim actively

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participates with its COVID-19 projects in the Innovative Medicines Initiative (IMI) of the European Union and the COVID-19 Therapeutics Accelerator, coordinated by the Bill & Melinda Gates Foundation.

- Bristol Myers Squibb (BMS) identified 1,000 compounds in its discovery library that they are making available to collaborators for screening for potential treatments for COVID-19. BMS is actively evaluating certain medicines in its portfolio that could be included in near-term clinical trials with a focus on agents impacting the inflammatory immune response associated with COVID-19.
- Chugai (daughter of Roche) is working to start a Phase III clinical trial in Japan with Actemra® Chugai filed a clinical trial notification with the Pharmaceuticals and Medical Devices Agency on April 8th, 2020. It hopes to enroll patients hospitalized with severe COVID-19 soon.
- Eli Lilly and AbCellera (Canadian biotech firm) have entered into an agreement to codevelop antibody products for the treatment and prevention of COVID-19. The collaboration will leverage AbCellera's rapid pandemic response platform, developed under the DARPA Pandemic Prevention Platform (P3) Program, and Lilly's global capabilities for rapid development, manufacturing and distribution of therapeutic antibodies.
- Eli Lilly and Company announced April 10, that it has entered into an agreement with the (United States) National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), to study baricitinib as an arm in NIAID's Adaptive COVID-19 Treatment Trial. The study will investigate the efficacy and safety of baricitinib as a potential treatment for hospitalized patients diagnosed with COVID-19, beginning this month in the U.S. with a planned expansion to additional sites including Europe and Asia. Results are expected within the next two months. Lilly will also advance LY3127804, an investigational selective monoclonal antibody against Angiopoietin 2 (Ang2), to Phase 2 testing in pneumonia patients hospitalized with COVID-19 who are at a higher risk of progressing to acute respiratory distress syndrome (ARDS). Ang2 is known to be elevated in ARDS patients and Lilly will test whether inhibiting the effects of Ang2 with a monoclonal antibody can reduce the progression to ARDS or the need for mechanical ventilation in COVID-19 patients. This trial will begin later this month at several U.S. centers.
- EFPIA is working with the Innovative Medicines Initiative (IMI) on potential actions to support collaborative research programs in order to fast-track the development of therapeutics.
- Eisai is participating in the COVID-19 Therapeutics Accelerator initiated by the Bill & Melinda Gates Foundation. The company is planning to provide its natural product libraries as well as its new vaccine adjuvant.
- Gilead has initiated two Phase 3 clinical trials of remdesivir in countries with high prevalence of COVID-19. The company is also supporting two Phase 3 trials in China and a global Phase 2 trial led by the U.S. National Institute of Allergy and Infectious Diseases. Gilead donated drug and provided scientific input for these studies. Gilead has provided remdesivir to physicians for compassionate use to treat several hundred severely ill patients with confirmed COVID-19, and has accelerated manufacturing of remdesivir at risk, in anticipation of potential future supply needs.
- GSK is entering into the new collaborative research effort, the COVID-19 Therapeutics Accelerator. The aim of the Accelerator is to bring pharmaceutical companies and expert academic institutions into coordinated research programs, with the aim of bringing the most promising molecules forward that could be used to treat cases of COVID-19. GSK will contribute by making available compounds from its libraries for screening for activity against COVID-19. In addition, GSK is evaluating its marketed pharmaceutical products and medicines in development to determine if any could be used beyond their current indications in response to the pandemic. Further, GSK is evaluating options to make available specialised laboratory space to help in research and testing of

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COVID-19. On 6 April 2020 GSK announced that it has entered into a collaboration with Vir Biotechnology to find coronavirus solutions. Vir Biotehnology is an immunology company based in San Francisco and our collaboration is focused on accelerating existing and identify new anti-viral anti-bodies that could help as therapeutic or preventative options to help address the current COVID-19 pandemic and future outbreaks. This includes two promising antibody candidates and, subject to regulatory review, we plan to proceed directly into a phase 2 clinical trial within the next three to five months.

- GSK and Vir Biotechnology, Inc. signed a binding agreement to enter into a collaboration to research and develop solutions for coronaviruses, including SARS-CoV-2, the virus that causes COVID-19. The collaboration will use Vir's proprietary monoclonal antibody platform technology to accelerate existing and identify new anti-viral antibodies that could be used as therapeutic or preventative options to help address the current COVID-19 pandemic and future outbreaks.
- GSK announced plans to collaborate with China's Xiamen Innovex on a potential vaccine to treat the COVID-19 coronavirus. The companies are testing a recombinant protein-based coronavirus vaccine candidate, which is being developed by Innovax with Xiamen University.
- Ipsen donated financial resources to the Institut Pasteur to support research on COVID-19. Since January, the Institut Pasteur has devoted a portion of its research to understanding the emerging COVID-19 virus, in terms of epidemiology, biological characteristics, pathogenicity.
- Johnson & Johnson, (10)(2e) is undertaking ongoing work with global partners to screen a library of existing antiviral molecules, with the aim of identifying compounds with promising antiviral activity against the novel coronavirus, SARS-CoV-2 (also known as 2019-nCoV). We are working to identify existing or new compounds with antiviral activity against SARS-CoV-2 that could contribute to providing immediate relief to the current outbreak. This work is being conducted in partnership with the Rega Institute for Medical Research (KU Leuven/University of Leuven), in Belgium.
- Merck: As part of the global effort to investigate potential therapeutics for COVID-19 and Merck's support of independent research, Merck recently donated a supply of interferon beta-1a (Rebif®) to the French Institut National de la Santé et de la Recherche Médicale (INSERM) following a request for use in a clinical trial. The trial is sponsored by INSERM and its launch has been announced by the French Health authorities on March 11.
- Merck is donating 290,000 units of its interferon beta-1a (Rebif®) to the WHO for use in their global SOLIDARITY trial which investigates several potential therapeutics for the treatment of COVID-19.
- Novartis announced that it has entered new collaborative research efforts such as the COVID-19 Therapeutics Accelerator, coordinated by the Bill & Melinda Gates Foundation, Wellcome, and Mastercard, as well as a COVID-19 directed partnership organized by the Innovative Medicines Initiative. Novartis is contributing by making available several compounds from its libraries that are considered suitable for in vitro antiviral testing. In addition, the company is rapidly evaluating other existing products to see if any could be utilized beyond their approved indications in response to the pandemic.
- Novartis plans to initiate a Phase III clinical trial in collaboration with Incyte to evaluate the use of Jakavi® (ruxolitinib) for treatment of a type of severe immune overreaction called cytokine storm that can lead to life-threatening respiratory complications in patients with COVID-19.
- Novartis announced it would conduct a 450-person study in the U.S. to determine if its malaria drug hydroxychloroquine can effectively treat Covid-19.
- Pfizer announced that it completed a preliminary assessment of certain antiviral compounds that were previously in development and that inhibited the replication of coronaviruses similar to the one causing COVID-19 in cultured cells. Pfizer is engaging with a third party to screen these compounds under an accelerated timeline and expects to have the results back by the end of March.

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- Pfizer also outlined a detailed 5-point action plan to battle COVID-19. The plan includes a commitment to sharing its clinical development and regulatory expertise to support other smaller biotech companies that are screening compounds or existing therapies for activity against the virus causing COVID-19.
- Pfizer shared preliminary data confirming the anti-SARS-CoV-1 compound shows antiviral activity against SARS-CoV-2. Pfizer will perform pre-clinical confirmatory studies, including further anti-viral profiling and assessment of the suitability of the lead molecule for IV administration clinically.
- Pfizer and the Liverpool School of Tropical Medicine's Respiratory Infection Clinical Research Group are launching two new studies to provide insights on the interaction between S. pneumoniae and SARS-CoV-2. The SAFER study and FASTER study will help demonstrate whether patients infected with COVID-19 have a higher risk of also developing pneumococcal pneumonia and if having both infections leads to more severe disease and poorer outcomes.
- Regeneron Pharmaceuticals announced an expanded agreement with the U.S. Department of Health and Human Services (HHS) to develop new treatments combating the novel coronavirus
- Regeneron Pharmaceuticals and Sanofi SA started a clinical program evaluating Kevzara, originally a drug to treat arthritis, in patients hospitalized with severe COVID-19. Kevzara is a fully-human monoclonal antibody that inhibits the interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor. IL-6 may play a role in driving the overactive inflammatory response in the lungs of patients who are severely or critically ill with COVID-19 infection.
- Roche's Actemra was approved by China on March 5 to treat Covid-19 patients with lung complications. Roche has donated nearly $2m-worth of Actemra to China to help the country manage the COVID-19 outbreak". Actemra has been on the European market since 2010 for treatment of several kinds of arthritis.
- Roche announced that they are working with the Food & Drug Administration (FDA) to initiate a Phase III clinical trial to evaluate the safety and efficacy of Actemra in hospitalised adult patients with severe COVID-19 pneumonia. This is the first global study of Actemra in this setting and is expected to begin enrolling as soon as possible in early April with a target of approximately 330 patients globally, including the US.
- Takeda announced that it is initiating the development of a drug to treat people infected with the novel coronavirus. The experimental drug would be derived from the blood of coronavirus patients who have recovered from the respiratory disease. In parallel, Takeda is also exploring whether currently marketed and pipeline products may be an effective treatment option for infected patients.
- Takeda together with CSL Behring set up a partnership bringing together world-leading plasma companies to focus on developing and delivering a hyperimmune immunoglobulin in the global fight against COVID-19.
- Teva is actively looking through its range of products to determine if it can help provide any products that may be relevant in addressing acute and substantial need during the COVID-19 crisis.

Source: https://www.ifpma.org/subtopics/novel-coronavirus-covid-19-industrys-rd-efforts/ and EFPIA member company information

Diagnostics:

- Abbott launched an antibody test for coronavirus and plans to ramp up manufacturing to produce 20 million tests by June.

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- AstraZeneca is accelerating the development of its diagnostic testing capabilities to scale-up screening and is also working in partnership with governments on existing screening programmes to supplement testing.
- Bayer is making more than 40 virus diagnostics devices available from its research operations to scale up Germany's COVID-19 analysis by several thousand tests daily.
- Novo Nordisk scientists are working in R&D laboratories to boost Denmark's COVID-19 testing capacity.
- Roche announced that the FDA issued an Emergency Use Authorization for its diagnostic kit cobas® SARS-CoV-2 Test, advancing coronavirus testing to meet urgent medical needs. Roche is committed to delivering as many tests as possible and is going to the limits of production capacity.
- Takeda is partnering with public entities and other pharmaceutical companies through the Innovative Medicines Initiative (IMI) in Europe to leverage collective expertise in the hope of developing diagnostics for COVID-19 as well as inhibitors to help prevent future outbreaks.
- UCB is working closely with the Belgian government to scale up COVID-19 testing capabilities. It is looking at similar possibilities in the UK.

Source: https://www.ifpma.org/subtopics/novel-coronavirus-covid-19-industrys-rd-efforts/ and EFPIA member company information

Vaccines Europe - List of projects for the development of a coronavirus vaccine (5 May)

- **CureVac** is developing a mRNA based prophylactic vaccine against SARS-CoV-2, funded by CEPI and in collaboration with CEPI. Curevac is preparing a clinical study that expects to start in early summer in Germany and Belgium. Curevac is in contact for scientific advice on this vaccine development with EMA, PEI (Germany) and with FAMHP (Belgium). The EU Commission has offered financial support to CureVac, to scale up development and production of a vaccine against the Coronavirus in Europe. More info here. CureVac's press release:
- **GSK** is supporting vaccine development by providing access to its pandemic vaccine adjuvant platform to selected institutions and companies with promising vaccine candidates. In doing this we are contributing to a coordinated effort, focusing on the most promising approaches to enable development of strong candidate vaccines for COVID-19. Access to our adjuvant technology is being provided through CEPI, the Coalition for Epidemic Preparedness Innovations or directly, in bilateral agreements. So far, we have announced two collaborations one with the University of Queensland and the second with Clover, a Chinese company and other collaborations are under discussion. In the pandemic flu setting, our adjuvant system has been shown to be antigen-sparing, i.e. less of the antigen is needed per dose to protect an individual than would be needed in a vaccine without the adjuvant included. If this is shown to be the case with our adjuvant system for COVID-19 vaccines, we would be able to protect more people, as less antigen would be needed per person, a crucial advantage in the case of a pandemic where high numbers of doses are needed for broad protection and manufacturing capacity is limited. GSK allies with Innovax for COVID-19 vaccine R&D project: GlaxoSmithKline has teamed up with Xiamen Innovax Biotech to evaluate a vaccine against the novel coronavirus behind the COVID-19 pandemic. The agreement gives Innovax access to a GSK adjuvant to enhance the immune response triggered by its recombinant protein-based vaccine.
- **Johnson & Johnson** has mobilised resources in response to the outbreak to develop a preventive vaccine candidate against this coronavirus, leveraging Janssen's AdVac® and PER.C6® technology, that provide the ability to rapidly upscale production of the optimal vaccine candidate. These are the

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same technologies that are used in the development and manufacturing of Janssen's investigational Ebola vaccine and are also used to construct the Company's Zika, RSV and HIV vaccine candidates. In addition, Johnson & Johnson is collaborating with regulators, healthcare organizations, institutions and communities worldwide to help ensure our research platforms, existing science and outbreak expertise can be maximized to stem this public health threat. Johnson & Johnson's efforts to expedite development and production of a vaccine are enhanced by the existing COVID-19 vaccine collaborations between (10)(2e) and the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) at the U.S. Department of Health & Human Services. On March 13, 2020, a new collaboration was announced with the Beth Israel Deaconess Medical Center (BIDMC) to support the development of a preventive vaccine candidate for COVID-19. The parties have commenced preclinical testing of multiple vaccine prospects, with the aim to identify by the end of the month a COVID-19 vaccine candidate for clinical trials.

Johnson & Johnson on 30th March announced the selection of a lead COVID-19 vaccine candidate from constructs it has been working on since January 2020; the significant expansion of the existing partnership between the (10)(2e) Pharmaceutical Companies of Johnson & Johnson and the Biomedical Advanced Research and Development Authority (BARDA); and the rapid scaling of the Company's manufacturing capacity with the goal of providing global supply of more than one billion doses of a vaccine. **The Company expects to initiate human clinical studies of its lead vaccine candidate at the latest by September 2020 and anticipates the first batches of a COVID-19 vaccine could be available for emergency use authorization in early 2021**, a substantially accelerated timeframe in comparison to the typical vaccine development process. More info here.

- **MSD** have deep expertise in vaccines and infectious diseases. As a science-driven company that aims to address some of the world's biggest health care challenges they are carefully monitoring the situation. As an initial step, based on the information available at this time, MSD has established a team of scientists to assess internally available vaccine assets for potential to impact the COVID-19 and related viruses.
- **Novavax** announced that it has identified an "ideal" coronavirus vaccine candidate — and is set to launch the first clinical human trial in mid-May. Novavax advances the development of novel COVID-19 vaccine, with the vaccine candidate derived from coronavirus spike (S) protein. Matrix-M™ adjuvant is expected to boost immune responses. On 10 March 2020, Novavax announced that CEPI, the Coalition for Epidemic Preparedness Innovations awarded an initial funding of $4 million to support Novavax' efforts to develop a COVID-19 vaccine. CEPI and Novavax are having ongoing discussions on additional funding from CEPI to address Novavax' costs through Phase 1.
  On 8 April 2020, Novavax announced that it has identified a coronavirus vaccine candidate, NVX-CoV2373, a stable, prefusion protein made using Novavax' proprietary nanoparticle technology, and will initiate a first-in-human trial in mid-May. **Novavax' press release.**
- **Pfizer** is working to advance their own potential antiviral therapies and is engaged with BioNTech on a potential mRNA coronavirus vaccine. The companies are scaling up production to potentially produce millions of vaccine doses by the end of the year — and hundreds of millions in 2021 — depending on how well their vaccine works and the course of regulatory approval. BioNTech is working on a number of vaccine candidates using mRNA platforms, and hopes to begin human trials this month. More info here.
- **Pfizer and BioNtech** issued a press release announcing that they have received regulatory approval from German authority, Paul Ehrlich Institute, to commence first phase 1/2 clinical trial of our COVID 19 vaccines. The trial is the first clinical trial of a COVID-19 vaccine candidate to start in Germany,

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and is part of a global development program. Pfizer and BioNTech will also conduct trials in the United States upon regulatory approval, which is expected shortly. More info here. On the 29 April, the BioNtech and Pfizer announce completion of dosing for first cohort of phase 1/2 trails of COVID-19 vaccine candidates in Germany. More info here.

- **Sanofi** announced in February 2020 a collaboration with the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services, to advance a novel COVID-19 vaccine candidate. Work is underway to leverage previous development of a SARS vaccine candidate using Sanofi's recombinant DNA technology. COVID-19 belongs to the same family of coronaviruses as SARS. Research materials can be produced relatively quickly for clinical testing because we have a licensed influenza vaccine based on this platform. Further, this technology has the advantage of being highly scalable, allowing Sanofi to potentially rapidly produce large quantities of the coronavirus antigen. Sanofi is also coordinating with the Coalition for Epidemic Preparedness Innovations (CEPI) and sharing its vaccine R&D experience and expertise to advance vaccine solution. Sanofi Pasteur and Translate Bio, a clinical-stage messenger RNA (mRNA) therapeutics company, will also collaborate to develop a novel mRNA vaccine for COVID-19. Public statement here.
- **Seqirus** is providing scientific and technical expertise and its well-established MF59 adjuvant technology to the University of Queensland in Australia to help fast-track the development of their CEPI-funded n-COV19 vaccine candidate using novel molecular-clamp technology.
- **Sanofi and GSK announce they are entering into a collaboration to develop an adjuvanted vaccine for COVID-19**, using innovative technology from both companies, to help address the ongoing pandemic. Definitive terms of the collaboration are expected to be finalised over the next few weeks. Sanofi will contribute its S-protein COVID-19 antigen, which is based on recombinant DNA technology. GSK will contribute its proven pandemic adjuvant technology to the collaboration. They plan to initiate phase I clinical trials in the second half of 2020 and, if successful and subject to regulatory considerations, aim to complete the development required for licensure in the second half of 2021. Considering the extraordinary humanitarian and financial challenge of the pandemic, both companies believe that global access to COVID-19 vaccines is a priority and are committed to making any vaccine that is developed through the collaboration affordable to the public and through mechanisms that offer fair access for people in all countries. More info here.
- **AstraZeneca and University of Oxford** joined forces to be responsible for the development, worldwide manufacturing and distribution of the vaccine, developed by the Jenner Institute and Oxford Vaccine Group, at the University of Oxford, if clinical trials prove successful. More info: here.

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