

## Highlights

### Pharmaceutical Strategy for Europe
***Fabio D'Atri***

The pharmaceutical strategy for Europe springs from the issues regarding the inadequate patient access and shortages of medicines and their affordability, from the necessity to ensure that the EU Regulatory framework continues to enable need-driven innovation and that the EU maintains its competitive position in the pharmaceutical field at world level.

The Covid 19 case has further highlighted these issues.

The approach of the European Commission is holistic, taking into account all the aspect of the pharmaceutical scene.

Collaboration is an essential aspect of the strategy. For this reason the European Commission has launched several consultation activities on the content of the EU pharmaceutical Strategy. All interested stakeholders have contributed, sending their concerns and suggestions. A workshop haa also been organised in July and all major aspects of the strategy have been discussed, like , for example, the prioritisation of unmet needs and the need to exchange of best practices on procurement and price and reimbursement.

The European Commission is now finalising a communication on the Strategy which is expected to be published by the end of November 2020. The various actions of the strategy will be implemented in the period 2021-2023.

Some of main targets of the strategy will be:

° to establish an efficient regulatory system to enable innovation
° to prioritise the unmet medical needs
° to ensure affordability of medicines and sustainability of the system

To look more in detail about this topic consult and freely download the presentation and the video recording here.



## Highlights

### The increased value of the EC consultation to promote the new strategy

*Viviana Giannuzzi, Enrico Bosone*

A public consultation is the best tool to involve the citizens, the patients and all the stakeholders in a transparent manner.

The Benzi Foundation efforts are greatly focused on the biomedical research, innovation and particularly in rare diseases. So, we have contributed with some suggestions to the public consultation released by the European Commission on the EU Pharmaceutical strategy as follows:

1) To foster GMP compliant factories in the EU, simplifying bureaucratic burden but increasing official controls
2) To implement a EU-wide marketing authorisation in order to really harmonise the availability of medicines across Europe
3) To make the legislative framework more adaptive to new technologies and use the artificial intelligence (AI) also for regulatory purposes
4) To provide R&D incentives/tax reductions in areas of unmet needs
5) To better co-ordinate multi-national trials, making the process of implementation faster
6) To increase the transparency on cost and price of innovative medicines
7) To exploit the new centralized P&R centralised procedure, used as “Emergency support Instrument” for Covid, also in special cases such as for ATMPs and orphan medicines in children

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## Highlights

### The European pharmaceutical system: strenghts and weaknesses. Specificities of rare diseases

***Francois Houyez***

The Orphan drug Regulation has been a great success, with 188 OMPs now available, but with some issues. In some cases, the OD Regulation has been used to obtain greater economic return. But what is more importanti is the fact the many patients with rare diseases are still without a valid therapy. Inequalities within rare diseases are still high.

Another issue is the high price that in some cases is a hurdle for the real availability in all the Countries in Europe.The OECD suggests to better target drugs whose development will not occur without additional incentives. So a good tool could be to increase incentives which stimulate research in lower prevalence diseases.

For the real availability of high price medicines some innovative tools could be used : an EU fund, a strong cooperation for joint procurement or the innovative agreements used in Australia for HCV or in Denmark for Cystic Fybrosis ( lump sum remuneration) and the DCF method (Nuijten 2018) to calibrate a sensible price.

Majority of OMPs are made in the EU but, to avoid shortages, we could use non profit manufacturers and/or resources and power to EMA to regulate medicine supplies, depending on the needs of each MS. For the repurposing of old medicines, the STAMP initiative can be implemented.To favour the early availability of innovative OMPs the compassionate use programs could be harmonised in the EU.

In some cases, the compulsory licences can be used. Presently it is used mainly in the est states of the Union. In general, the cooperation should come before the competition to cover also the rare diseases with lower prevalence.

In conclusion now we have the chance to improve the OD Regulation, which has been an important tool to cure many patients with rare diseases, but needs a further step to be more useful.

To look more in detail about this topic consult and freely download the presentation and the video recording here.



## Highlights

## Company perspective

Martin F. Ryser

Since the early days of the outbreak, Johnson & Johnson has been working with industry partners, governments and health authorities to help end the fast-moving COVID-19 pandemic through the development of a preventive vaccine candidate against SARS-CoV-2. The search for a vaccine is being progressed by partnerships and collaborations including those between the Janssen Pharmaceutical Companies of Johnson & Johnson and the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health & Human Services, and the Beth Israel Deaconess Medical Center (BIDMC).

Johnson & Johnson announced on March 30, 2020 that a lead COVID-19 vaccine candidate, Ad26.COV2.S (with two back-ups) has been identified from constructs our scientists had been working on since January 2020. Our Phase 1/2a first-in-human clinical trial of the Janssen COVID-19 vaccine candidate in healthy volunteers, has commenced in the United States and Belgium. We have also initiated a Phase 2a study in the Netherlands, Spain and Germany, and a Phase 1 study in Japan. We launched our Phase 3 trial (ENSEMBLE) for Janssen's COVID-19 vaccine candidate in September 2020, following positive interim results from the Phase 1/2a clinical study, which demonstrated that the safety profile and immunogenicity after a single vaccination were supportive of further development.

Johnson & Johnson is committed to bringing an affordable COVID-19 vaccine to the public on a not-for-profit basis for emergency pandemic use. We have ramped up our R&D processes to unprecedented levels, and our teams are working tirelessly to provide global access to Janssen's COVID-19 vaccine candidate, if proven to be safe and effective.

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## Highlights

## Impact of COVID-19 on Clinical Trials. New approaches that can be taken for future trials

**Martine Dehlinger-Kremer**

Dr Dehlinger-Kremer reported on the situation of clinical research and how it was impacted by the COVID-19 pandemic. Ongoing clinical trials faced challenges related to operational aspects (e.g. lack of resources at sites, difficulties to access sites) but also to a lack of validated endpoints suitable for remote data collection. As a consequence, numerous companies did set their trials on hold to avoid a change in endpoints. Examples illustrating how research was adapting by moving towards decentralised clinical trials (DCTs) in order to ensure trial participants' safety, e.g., allowing them to participate remotely through tools such telemedicine and wearable technology.

Another alternative presented were trials with a combination of home and site visits. Positive effects included reduced study fatigue, elimination of parents' fear to travel to sites during the COVID-19 pandemic, no missed visits, and a positive impact on patient retention. However, today, not all sites allow home health care when the medicine is to be prepared by a hospital pharmacy. Limitations observed at some sites were the non-existence of accessible electronic medical records, limited equipment at the site such as e.g., webcam availability and due to the emergency status, site staff availability was reduced.

Positive aspects of remote monitoring included freeing up time for data review (no travel time required), and a reduction in trial travel costs.

From the experiences gained during the pandemic, some new operational approaches could/should be taken forward in the future post pandemic. A prerequisite would be to have endpoints to be adapted for remote monitoring and regulatory pathways adapted to the use of new technology in clinical trials.

To look more in detail about this topic consult and freely download the presentation and the video recording here.



## Highlights

### Orphan Regulation faced with changes in the EU pharmaceutical system

***Viviana Giannuzzi***

The European Pharmaceutical Strategy recently released includes strengths and weaknesses of the legal instruments. The European Commission (EC) is preparing the review of the legislation on medicines for rare diseases and children: the Orphan and Paediatric Regulations. What emerges from the EC report is that even if great efforts have been made in Europe on the availability of drugs for rare diseases thanks to the incentives issued by the regulation, on the other hand Research & Development has not been adequately supported in areas where the need for medicines is greatest and completing the Research & Development process still remains a challenging issue for an orphan medicinal product.

The following actions might be integrated in the Regulation revision:

- *Training to make academia and other applicants expert*
- *Economic support to R&D in terms of tax discounts*
- *More correlation with Paediatric Regulation*
- *Methodology to gain the reliable evidence supporting the Marketing Authorisation considering data sharing initiatives of utmost importance for rare diseases.*

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**XIII FORESIGHT TRAINING COURSE**

***Challenges for Researchers and Regulators facing the pandemic crisis***

***23 October 2020***

## Highlights

**Ethical concerns and risks in health emergency: patients protection and fundamental rights**
*Annagrazia ALTAVILLA*

The emergency situation, such as COVID-19 pandemic, when healthcare systems can be greatly affected, the number of severe cases raised major ethical challenges in providing healthcare to patients, and decisions are taken under pressure in a context of uncertainty and scarce resources, demonstrates the fundamental importance of everyone's right to health protection. The main objective of governments and EU actions has been to guarantee a non-discriminatory access to medical care while strengthening and maintaining the integrity of health care systems, trying at the same time, to safeguard fundamental freedoms and economic interests.

All the main stakeholders and international institutions agreed on the fact that, in any case, specific circumstances can compromise the compliance of the actions with fundamental rights. Internationally recognized ethical standards and principles (such as the principles of autonomy, beneficence, non-maleficence and justice) must always be respected.

To this aim, the EU adopted a very innovative emergency support instrument that provides financial support for ensuring provision of medical equipment, regulating exports of key supplies from the EU, increasing the production with European industry, ensuring the transport of medical items, the transfer of medical personnel and finally to training multidisciplinary pool of healthcare professionals, especially for intensive care units. A new pharmaceuticals strategy has been submitted to public consultation with the aim to ensure Europe's supply of safe and affordable medicines, meet patients' needs providing all patients with access to optimal care, to reduce the EU's dependency on imports from third-countries, making medicines, including vaccines, available under all circumstances.

More recently, an EU-wide tracing system has been released to ensure that coronavirus contact and tracing apps developed at national levels can 'talk to each other'. The system went live in october with the first wave of national apps now linked through this service. This "decentralised" system, in combination with the Gateway Services and a server hosted in the Commission's own data centre in Luxembourg, enables these apps to be used across borders while allowing citizens' personal data are fully protected.

In this context, to help member states in applying European human rights and ethical standards in the biomedical field, it should be essential to support capacity building programs. Cross-sectoral and multidisciplinary co-operation should be promoted to avoid fundamental rights infringements (especially where vulnerable populations e.g. children/elderly are involved). Finally, to be successful in the development of efficient solutions it should be crucial to build trust, closely involving the civil society and the general public.

To look more in detail about this topic consult and freely download the presentation and the video recording here.



## Highlights

### Questions and Answers, Discussion

1. **Centralised negotiation also for procurement and pricing of ATMPs and OMPs in children? (Bosone)**

   **D'Atri** explains that the common procurement procedure for remdesivir, vaccines and other COVID treatment products has been one of the positive results of the pandemic. However, pricing of medicinal products is a completely national competence and the EU can act only with the agreement of Member States To trigger a common procurement process the agreement of Member States is necessary. In the past, triggering such procedure had not been successful due to the lack of sufficient interest.

2. **Priority for rare diseases and OMPs**

   This issue has been agreed by many Speakers: it will be an important topic for the new OMP Regulation.

3. **EUnetHTA also conducts rolling reviews for medicines to treat COVID-19 and vaccines. Are the EMA rolling reviews also made public? (Houyez)**

   **Cavaleri**: so far the rolling reviews are still confident but, as soon as we reach an opinion, they will be published

4. **How many PIPs have been already applied for COVID products? How many have been granted? (Ceci)**

   **Cavaleri**: Three of them are under discussion but we expect to have many others very soon.

5. **Could we dream of a time where drugs can follow a similar accelerated approval process as seen for COVID-19 vaccines? Thinking in particular of rare diseases with unmet medical need (Leary**)

   **Cavaleri**: We agree but we cannot do this procedure systematically because it has been very demanding in term of human resources.



6. **Considering that the COVID-19 study is enrolling 60000 people in a short time, has JC foreseen any use of innovative technologies to support this large recruiting effort and the conduction of the trial? (F. Bonifazi)**

   **Ryser**: Yes, we have used innovative technologies with the objective to rapidly activate trials in different countries. IT has been also useful focusing diverse populations into the trials

7. **How the Emergency readiness was arranged for home visits? For Phase II there should be near-by emergency readiness available and a doctor – not only the nurse (Lepola)**

   **Kremer**: answer to be given afterwards because it needs a specific competence.

8. **Do you think that the the new operational approaches may or should remain in place after the pandemic? (F. Bonifazi)**

   **Kremer**: Not for all of them but for some of them, for example how to recruit patients and for retention of patients, because they can save some travels to the sites.

9. **Is the use of remote procedures associated to a lower cost? Which are the more experienced difficulties to move towards remote processes? Type of diseases? Populations? (Ceci)**

   **Kremer**: yes, for example travel costs are reduced but you have other costs: for example the validation of the tools. For sure these new tools are convenient for elderly people, who can save the travels. In addition of this, the new tools are not adapted for all the diseases, depending on the endpoints which have to be validated.

10. **Does 5G technology helps to increase the safety of clinical data (to avoid hackers) and, in the same time, facilitate the activities of the Operators, reducing the burden of the complexity of GCP in clinical trials? (Bosone)**

    **Kremer:** answer to be given afterwards because it needs a specific competence.

11. **How difficult is to work in different regulatory and clinical context such as US and EU? Which framework is more challenging in your experience? (Ceci)**

    **Gambotto:** in general, the translational part is the more difficult work we must do for the regulatory approvals. The regulators should put all the different pieces together, when there is a



good scientific rationale. If they should take into account the common correlated data, we could skip some of the tests. This action could be useful also for the orphan drugs which are studied by the academia.

12. **The vaccine you develop seems very promising. Would you not be interested to collaborate with industry? (Kremer)**

    **Gambotto:** we are open to collaborate with industry, particularly if the technology has the same base, as in case of adenovirus.

13. **Do you know if somebody is against the AI use? New luddistic groups? If yes, why are they against AI (privacy?) and which good reasons and tools to address their concerns? (Bosone)**

    **Mazzi:** AI is debated because on the one hand its use can be undoubtedly beneficial and desirable for many sectors, while at the same time it raises a number of concerns, especially regarding the socioeconomic consequences of its use. Indeed, the number of initiatives concerning the ethical use of AI is growing. These initiatives by far consist of soft law tools, such as code of conducts and best practices addressing challenges related for example to biases, accountability, fairness and yes, privacy. In fact, AI is "fed" with data and its potential is directly proportional to quality and quantity of data. Not only, but the logic behind certain AI output is also not readable, due to the so-called "black-box" phenomenon. Moreover, when it comes to healthcare, AI decisions potentially impact on people's lives and they are based on sensitive data. In this sense, compliance with data protection law plays an important role in safeguarding individuals' right and building a trust relationship between AI developers and users, and in Europe we have one of the most advanced standards from a privacy perspective, considering the level of rights recognition and protection that the GDPR ensures to data subjects.

14. **How can we mitigate the relevant problems underlined by Marek, regarding the care of children during pandemic? (Bosone)**

    **Migdal:** we should improve cooperation and coordination of our works to improve the situation.

To look more in detail about the Q&A session consult and freely download the video recording here.



## Highlights

## Research and Innovation for New and Advanced Medicines: the Role of Artificial intelligence

***Francesca Mazzi***

Artificial intelligence ("AI") is increasingly engaged and extremely promising in the healthcare sector. AI applications in healthcare range from personalised medicine to drug discovery and repurposing. Nonetheless, the use of AI raises a number of challenges.

Some of them are ethics-related concerns, to name a few: fairness of algorithms, level of data protection ensured to data subjects, accountability, explainability.

To this end, a considerable number of initiatives aimed at building frameworks for ethical AI based on shared principles recently arose. These initiatives focus on both technological and theoretical aspects and are shaping policies through a bottom-up approach for example encouraging code of conducts and best practices. Despite the desirability of such initiatives, the hypothesis of a top-down approach such as a regulatory intervention aligned with the shared principles is not, and should not, be disregarded.

Some other concerns relate to the implications of the use of AI in the pharmaceutical sector. Indeed, AI is amongst others often engaged in the research and development process for the creation of new drugs. Such engagement might challenge fundamentals of patent law and affect patentability of new drugs in principle. Moreover, the increasing relevance of data to "feed" AI and the types of investments required in relation to such technology might create barriers into entry for new businesses in the pharmaceutical market and a further concentration of the market power, amongst others based on the availability of data.

In this sense, it seems desirable to adopt adequate measures to incentivise transparency and data sharing, in light of the open access policy encouraged by the European Commission, and to work towards a sustainable business model which is not only environmentally and socially but also private-and-public-friendly, aimed at fostering innovation in light of public health in the age of AI.

To look more in detail all the contributions shared during the Course, you can freely consult the presentations and the video recordings here.