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Pharmacovigilance in the 2020s, the Past and the Future.

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In September 2017, the EUCROF Pharmacovigilance (PV) Working Group published a paper titled: *" Pharmacovigilance in 2020: Boldly Shaping the Future An overview. Part 1: Where we are"* (https://www.eucrof.eu/images/Documents/Future_of_PV_Outsourcing_PART_1_-_1_SEP_2017.pdf)

This paper contained a series of "predictions" regarding the possible scenarios involving the PV field in the 2020s.
Now, 5 years later and more than 2 years into the decade, the members of the PV working group thought it may be interesting to look back at those predictions and see where they were right and where they went wrong, taking into account the foreseeable and not foreseeable occurrences of the past few years.

The Authors would also welcome comments and criticism from the readers, with the possibility of starting a discussion (or, even better, a debate) leading to another set of predictions and – hopefully – to another similar paper a few years from now.

The most relevant predictions contained in the paper are listed in the following paragraphs *(in italics)*, along with the Authors' opinion on their correctness.

1. *The role of PV is becoming more and more relevant and strategic in the pharmaceutical industry.*

   ALMOST CORRECT, BUT NOT THERE YET.
   In fact, in the paper it was predicted that PV departments would be involved in a succession of strategic decisions within their organizations and were going to operate in close conjunction with executive management, on top of the "external" obligations emanating from national, regional and international regulatory bodies.
   This was going to increase the pressure on these departments, but it was also going to create new openings for PV experts who can now play a more significant strategic role in their organisations. Due to the growing importance of PV in the business world, one person even dared to ask at a DIA meeting: "*Are we ready for a CPVO (Chief Pharmacovigilance Officer)*?".
   It meant that, in the original prediction, PV professionals were going to have a greater say in setting overall company direction at the highest levels of the pharmaceutical industry. PV has not become one of the primary strategic drivers yet, but the increasing number of

inspections in the EU and in the rest of the world, has put PV on the agenda again. The backlog of inspections due to the impact of the pandemics is probably going to emphasize this trend, at least in the next couple of years.
It should be pointed out also that the approach to PV differs a lot from company to company. You can observe, in fact, a big difference across pharma companies, regardless of their size (from biggest to smallest).
Some treat PV purely as a necessary compliance function, whereas others have embedded PV on a much more strategic level in the higher ranks of their company, seeing it as competitive advantage to have good benefit/risk management and good safety reputation towards their patients.
This can be observed e.g. also by the level of authority granted to their EU QPPVs.

2. *The new regulatory requirements have considerably increased the workload of PV. The complexity of PV environment was going to lead to a growth in outsourcing of PV-related services.*
Delegating (wholly or in part) PV activities to organisations with specialist knowledge and expertise would become the most cost-effective solution for companies.

CORRECT
Due to their complexity and ever-increasing volume, along with the necessity to contain costs, PV-related services have become increasingly outsourced.
The global pharmacovigilance outsourcing market size was valued at USD 2.8 billion in 2017 and is expected to witness 15.7% CAGR (Compound Annual Growth Rate) from 2018 to 2024. A study of pharmacovigilance deployments has also shown that substantial cost savings of 30-40% can be made by outsourcing pharmacovigilance.
(https://cambreg.co.uk/pharmacovigilance-services/pharmacovigilance-outsourcing/)
Finally, The global pharmacovigilance outsourcing market is projected to grow from USD 4.2 billion in 2021 to USD 10.9 billion by 2026 at a CAGR (Compound Annual Growth Rate) value of 16.7%. (https://www.globalmarketestimates.com/market-report/pharmacovigilance-outsourcing-market-3410)

As a result, the most cost-effective option for most businesses has been to outsource their PV activities, either entirely or in part, to companies that have specialized knowledge and experience in this field and can be more cost/effective. This has led also to extensive "offshoring", with mixed results.
The past few years have seen a steep increase in the amount or human and/or economic resources devoted to PV and Drug Safety, but this increase has probably not reached a plateau yet.
Presently, outsourcing is used in small and medium companies as a means to comply with all their existing obligations, but it is also used by large and very large organizations for time and resource consuming activities, such as for example case processing, data management and literature searches.

3. *The focus of PV work has changed from simple "event counting" to "risk management" and this trend will continue.*

   CORRECT
   The starting point of this change could be placed between 2015 and 2016, when both EFPIA and EMA (through the voice of their top executives) confirmed that complying with the existing obligations in terms of timeliness, completeness and correctness of reporting of safety data was no longer sufficient and that all stakeholders would have to take a much more "proactive" approach, with the objective of preventing as much as possible the risks connected with the marketing of any drug and to increase its benefit/risk ratio.
   The focus was therefore going to shift from "collecting data" to "using data". Signal detection and management, as well as Risk Management Plans (RMPs), are now considered to be cornerstones of pharmacovigilance, but now the trend is toward making the best possible use of all the available data in the realm of PV and it is quite likely that the near future will see the development of initiatives based for example on Big Data.
   Here the situation is still evolving.
   On one side, in fact, social media have been considered as relatively unimportant as far as the collection of PV related information is concerned (see also Point 5).
   On the other side, Patient Support Programs (PSPs) have become more and more widespread and data coming from this source should probably be managed differently from the traditional sources (trials and PMS) in order to avoid both an unnecessary workload and the creation of unwanted "noise".

4. *Companies will be increasingly viewing PV as less of costly necessity and financial burden and more of a possible source of savings and even revenue potential, for example through the development of products that have a better safety profile, PV will allow MAHs not only to be compliant with existing and future regulations (no small feat in itself), but also to gain a competitive edge.*

   PARTLY CORRECT.
   As stated in a previous point, the importance of PV has grown further in the past few years. Executive management has realized that PV may have a significant impact on the bottom line of a company (both positive and negative). However, the role of PV is still more "supportive" than "strategic" and will probably remain as such, unless there are some unexpected occurrences (such as for example the "statins scandal") that may lead to radical changes in the regulations. There are no "Chief PV Officers" in pharma companies now, with possibly very few exceptions, even though this may be a useful development, especially in an environment that is becoming more and more competitive.

5. *The new challenges instigated by web and social listening or by the fact that regions outside of the EU, such as Eurasia or the Arab countries, will become more focused on risk management, and will require a more holistic approach to PV.*

   DIFFICULT TO SAY
   The geopolitical and social situation has changed very rapidly and nobody could have predicted the occurrence of a pandemics that probably changed forever our way of working and of a war that will surely affect for a long time the relationship between the Eurasian Economic Union

and the rest of the world. In 2017 the trend appeared to be toward a convergence of the positions of the different "blocks", at least as far as PV was concerned.
Presently it is almost impossible to tell whether this – or the exact opposite – will happen. As far as the "social" situation is concerned, it is quite sure that the sources of PV related information will change and evolve and the means to exploit them will have to change as well. A clear example is given by the role of social media (e.g. Facebook, Twitter, etc.) and by the question whether social media have a role as a useful and reliable source of PV information. In fact, as the Authors already reported in two recent papers on the subject, in less than two years, social networks went from being hailed as an innovative an indispensable source of knowledge on drug safety to a secondary and optional source that "performs poorly and cannot be recommended at the expense of other pharmacovigilance activities".
On the other hand, wearable devices (iPhones, etc.) have already been used as tools to collect vast amounts of clinical information, both on efficacy and safety of drugs (https://www.eucrof.eu/news-eucrof/latest-news/24-09-artificial-intelligence-ai-in-pharmacovigilance-do-we-really-need-it) .

6. *PV managers will likely have to become "knowledge managers" and be able to exploit in the most effective way the new available technologies. PV is going to become even more cross-functional, playing an increasingly important role across the life cycle of a drug.*

PARTIALLY CORRECT

In 2017 the application of advanced technologies and approaches such as Data Science, Machine Learning and Artificial Intelligence seemed to be much nearer. The publication of the results in 2018 of a joint research project between IBM and Celgene, which pitted the brainpower of Watson (a computer program capable of winning a TV quiz) against PV case processing, made many people believe that the days of Safety Officers were counted (https://pubmed.ncbi.nlm.nih.gov/30546259/).
Instead, as of today, there are case processing tasks (such as causality assessment and adverse event detection) where a machine can score around 75%, which is an impressive value but not (yet) something that could be used in an operational setting.
Regulatory Authorities moreover are still considering and discussing what would be needed in order to confirm the reliability of these new technologies. Already applied technologies focus on rather basic automations of relatively straightforward parts of PV case processing. They can provide important efficiency improvements but are far from end-to-end automated solutions. Nevertheless, the technology field is progressing very rapidly and there are already areas where machine based (or aided) approach could originate significant increase in efficiency.
For example, a new AI based environment, Chat GPT (an AI chatbot, using lay language dialog model for providing accurate information) entered the arena at the end of 2022. Although still under development with many recognised limitations, this AI tool is already drawing a lot of attention and is being hailed in many circles as "the new Google" (both as a search engine and as a way of collecting and processing data on content and user behaviour).
On the other hand, many are still very sceptical or even consider the widespread use of AI as "extremely dangerous".
Chat GPT and its potential competitors that came even later, have not been fully explored yet for the potential use of these technologies in PV activities, but may be interesting to consider.
It can be expected, therefore, that PV managers will still need additional knowledge or counselling in advanced digital technologies along with continuous updates, if they want to be

able to take adequate and informed decisions as far as if, when and to what extent these technologies should be considered and implemented in the PV workflow.

7. *The adoption of a proactive safety approach integrated as much as possible on top and across departments/divisions, but with provisions to include also affiliates and partners/vendors.*

CORRECT
As previously stated, PV has become a transversal set of activities, which involve not only the PV Department but essentially the whole company, including Sales Representatives (who are now required to have training in PV and to be able to collect and report safety issue) and partners/vendors (who are required to sign Safety Data Exchange Agreements). It is safe to assume that this trend will continue and will lead to a further increase of the relevance of PV/Drug Safety in all pharma companies.

8. This complexity has led to a growth in outsourcing of PV-related services. For most companies, delegating (wholly or in part) PV activities to organisations with specialist knowledge and expertise will become the most cost-effective solution.

CORRECT

As already stated in Point 2 (referring to the consequences of new regulatory requirements), the trend of the market has been towards outsourcing PV/Drug Safety activities to external organization, both small and large, creating a relevant niche for entrepreneurs. It is also quite likely that this trend will continue in the foreseeable future.

CONCLUSIONS

Predicting the future is always a challenging exercise, but it is an exercise in which practically all Mankind had indulged in the past millennia.
Without taking things (and themselves…) too seriously, the Authors are rather satisfied of their ability to predict oncoming events and situations in their line of business.
Some events that had an impact on the situation (such as for example the COVID pandemic, which called for an emergency approach to PV and also increased the level of awareness of the general population about the benefit/risk ratio of drugs) were completely unpredictable five years ago and the occurrence of these unforeseeable factors is something that makes predictions always difficult and somewhat aleatory.

The PV scenario, in fact, has evolved along the expected lines, even though not at the expected velocity, especially as far as the technological advancements were concerned (Big Data, Social Media, AI, automation, etc.).
PV therefore still represents one of “the places to be” in the Pharma Business.
As previously stated, the Authors would welcome the opinions, the contributions and the criticism of the readers, which can be sent to the corresponding Authors.