PHARMACOVIGILANCE REGULATORY AFFAIRS

2020

PHARMACOVIGILANCE AND REGULATORY AFFAIRS A LOOK AHEAD

Part of Proventa International's EU Pharmacovigilance and Reg Affairs Strategy Meetings
2019 Radisson Blu Zurich Airport, Switzerland - October 15, 16 2019

Attendee Statistics Who Went and What They're Investing In
The Top Strategic Challenges for PV and Reg Affairs, 2020 and Beyond
Highlights from All Our Tracks
An Expert Look at the Next Five Years

INTRODUCTION

Proventa's complimentary meetings around pharmacovigilance on one hand and regulatory affairs on the other have now concluded for another year. Both events were huge successes, providing delegates with a valuable and unique roundtable format to discuss key challenges and solutions with their peers as well as a perfect space to network and connect with other experts and leading figures in their industry,

Talk topics in both events focused on real, cutting-edge issues in the pharma space. In Proventa's PV event, experts discussed pragmatic PV disruption and AI in ICSR processing, while in Regulatory Affairs topics included regulatory information as part of digital transformation, and effective labelling measures in response to post-marketing safety surveillance.

THE FUTURE OF PV AND REGULATORY AFFAIRS

Highlights of the recent events are only one part of this report's objective. In writing this we also hope to provide even more useful material that looks at the future of the two sectors, with information not only on what our delegates are currently investing in but expert opinion from facilitators at our recent events discussing how the two areas will develop over the next five years.

There is a wealth and variety of information packed into the pages of this report: we hope you find them of interest and use, and enjoy your time reading.

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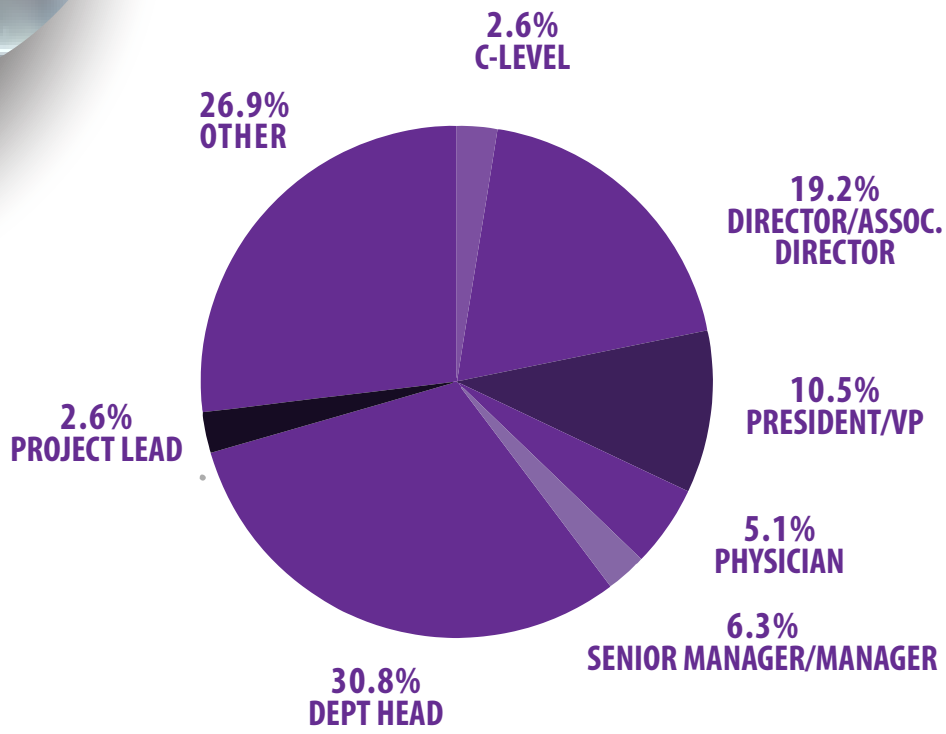
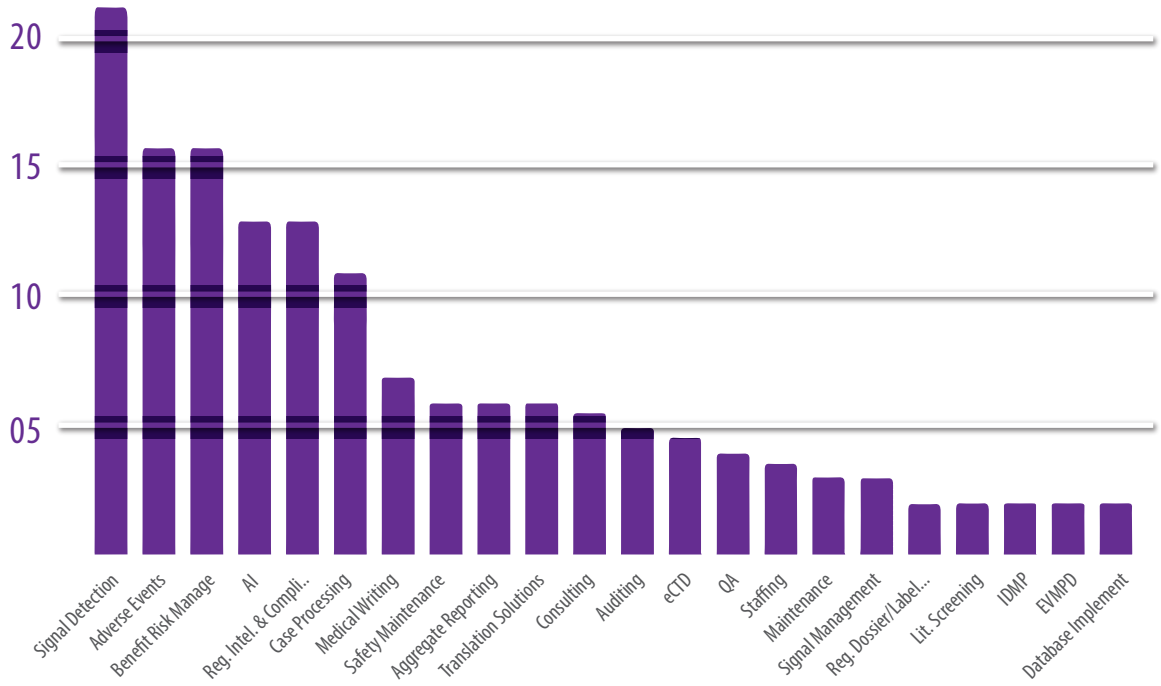
THE STATISTICS: ATTENDEE BREAKDOWN PHARMACOVIGILANCE





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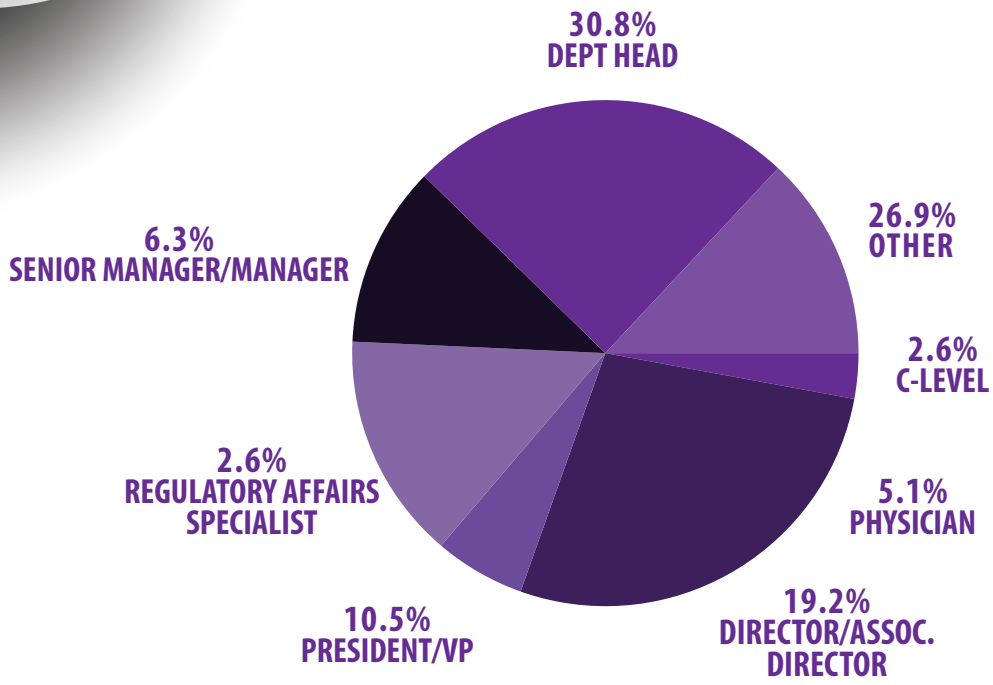
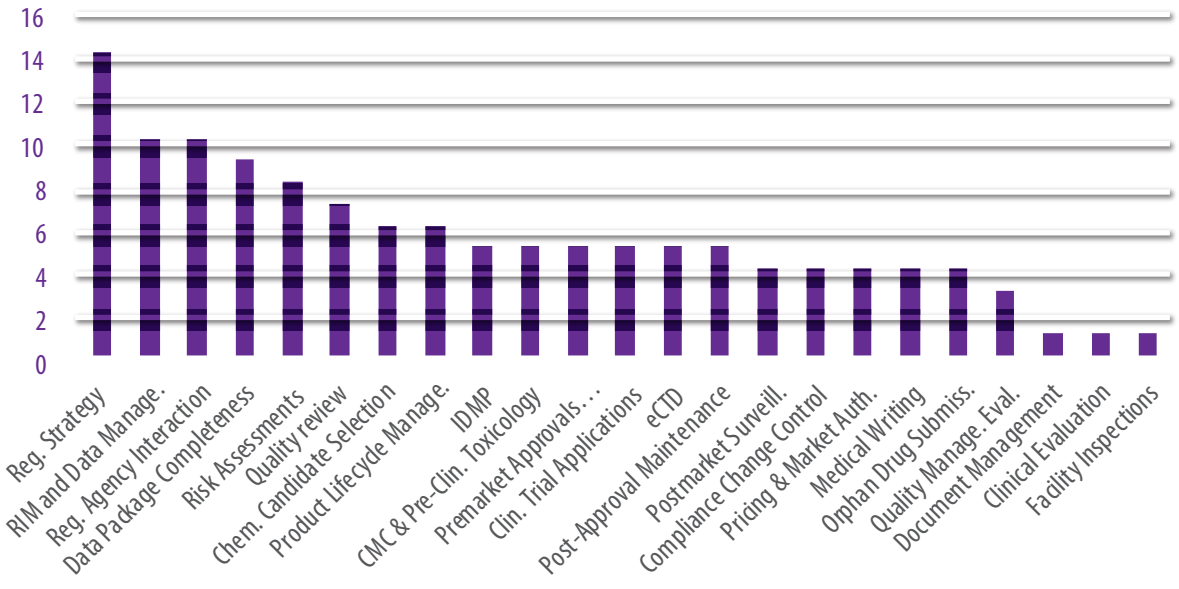




20 EVENT 19 HIGHLIGHTS

PHARMACOVIGILANCE

The 2019 Pharmacovigilance Strategy Meeting consisted of four tracks suited for almost every one of our professional delegates' interests. The day's tracks were: signal detection/management; technology/risk management and real world evidence; adverse events and patient-centricity. While every track showcased fantastic roundtables on forward-thinking topics, we present here some of the real highlights of the day, and the discussions within them.

ADVERSE EVENTS

The first track, on adverse events, kicked off with a roundtable facilitated by Maria Burian, Director of Translational Medicine Neuroscience at UCB. Her discussion focused on coalition before adverse event monitoring and drug surveillance, and began by noting that while last year was productive for new drug approvals, drug safety is falling behind, with only 1% of R&D expenses spent on safety. This is despite the fact that of the 90% of drug failures, 25% come from safety-related issues.

Some of the points that arose from this discussion included:
- while both patients and pharma companies speak with one voice over the need for speed in drug development, this increased process means less evidence for each approved drug
- risk management plans are hugely useful in R&D, providing further evidence and security for regulators, giving weight to proposals and allowing for the possibility of identifying future problems
- pharma companies vary on the extent that they run patient safety days or training; however, there is an uptake in SAEs and expert awareness thereafter
- while AE-reporting apps can see the problem of duplication and "over-reporting", given only 5-10% of AEs are reported generally the delegates agreed this wasn't necessarily a big issue. However, due to the fact that often only aggregated data is stored in apps, the potential for false signals is strong

After this, Nicole Radewic-Pahl of Adis Business Intelligence facilitated a discussion on harmonising literature monitoring, before Karsten Lollike of Novo Nordisk wrapped up the track with a roundtable focusing on discovering solutions for drug counterfeiting issues and analysing viable measures to combat and protect consumers.

In this final track roundtable of the day, participants discussed the overlap and difference in the definition of counterfeit and falsified medicines, as well as four elements of the Falsified Medicines Directive: safety, supply chain & good distribution practice, active substance and excipients, and internet sales. One key point to come from the roundtable was an expression of concern over how few citizens know on sight the EMA-supported internet pharmacy logo, with several delegates also expressing a lack of knowledge in the area.

TECHNOLOGY/RISK MANAGEMENT & REAL-WORLD EVIDENCE

Pilar Carrero of Novo Nordisk facilitated the first roundtable of this track, looking at ICSR processing ith the presence of AI. She was followed by Amr Khedr, International Medical Safety Head at Janssen, whose roundtable chose to focus on monitoring the effectiveness of risk management measures.

Beginning by discussing how different pharma companies run their risk management processes and ensure patient compliance, the talk moved on to talking about what should be captured. Delegates agreed that building an understanding of risk management both with patients and within companies would see AE reporting increase immediately.

The discussion then moved on to risk management technology, including its uses and downsides, before concluding with speculations on the need to increase the benefit/risk profile of a product, rather than safety.

Some of the key ideas that came out of this roundtable included that:

- it was widely agreed that while risk management profiles in most companies capture only additional or extraneous AEs, more focus should be levelled at persistent or "normal" patient effects - while a persistent, everyday headache would not be captured by most risk management policies, it will have a huge impact on the wellbeing of the patient
- the varied geographic burden of risk management evidence is challenging for many companies, with considerable quantities of information required in the U.S. while comparatively little is requested by the E.M.A
- while wearable patient technology, such as Apple Watches, fulfil regulatory requirements and are useful to gather data on serious cases of adverse effects, it was generally agreed that they are of much less importance for minor cases, where they were generally not required

SIGNAL DETECTION/SIGNAL MANAGEMENT

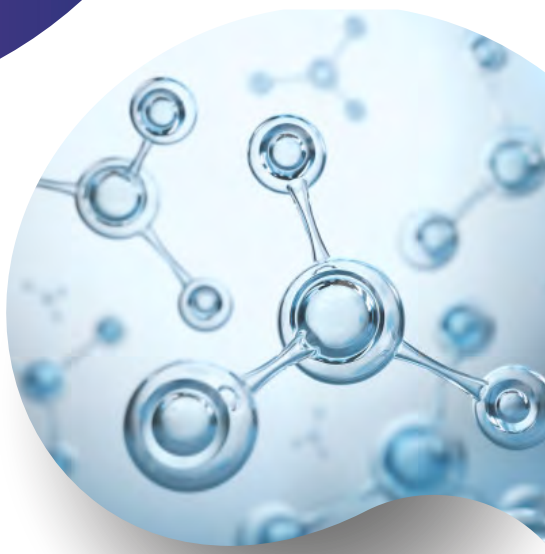
The day's signal detection and management track began with a discussion on meeting the needs of all stakeholders in signal management, hosted by Takeda's Fatima Bhayat. After that, Raj More of RxLogix Corporation led a discussion on pragmatically viewing disruption in PV technology.

The final talk of the day was facilitated by Adrian Panaite of CSL Behring, whose roundtable focused on identifying the latest development and innovation approaches for effective signal management. In particularly, its aims were to look, among other things, at the latest developments for effective signal management, how it is being done in different countries, and how it could be handled best be professionals in the area.

The roundtable began by discussing the continuing discovery of false positive signals, even though all sources are being captured with more data than ever. It was decided that quality, not quantity, was what was important in signal detection, with fewer rather than more signals needed. It was noted that man signals are received too early, with early capture not always the best solution.
Use of social media was the next topic discussed. Delegates noted that it is difficult to collaborate actively with sites such as Facebook, with limited access granted to pharma companies. While AI is in theory a useful tool for sorting and analysing social media data, it was agreed that misinterpretation of signals and data privacy laws are a major setback. Meanwhile, speculations that an auto-algorithm could be placed in a database to activate when a certain threshold of information on an AE was reached were ultimately vetoed, as just creating more data to be analysed.

The overarching conclusion of the roundtable was that "we must go back to the basics, and the basics are data": investment must be placed in analysis, storage and pharmacovigilance.

The session ended with a discussion about robotic process automation, a big opportunity that is eminently more reachable than spurious future ideas about AI and that can populate forms and compile AE information from medical records and other sources to send to authorities. The technology was enthusiastically welcomed as both useful and enactable in the near future.



PATIENT-CENTRICITY

The last of PV's tracks, patient-centricity, opened with a roundtable by Heinz Weidenthaler of Bavarian Nordic, on ensuring patient safety in rare disease trials, focusing on real-time proactive approaches versus conventional retrospective reporting. He was followed by Amr Khedr of Janssen, who gave roundtable this time on PROs' involvement in rare disease trial design, and how social networks build up patient engagement and patient experience.

After this, Omer de Mol, of Santhera Pharmaceuticals, facilitated a discussion on registries and other types of post-approval studies as support to patient-centric approaches, before Pavel Garkaviy, Associate Medical Director at AstraZeneca, facilitated a fantastic roundtable on how patient-centric ePRO solutions help boost study compliance and completion. Some of the takeaways from this session include:

- Patient safety must always be the first consideration
- Patient education is hugely important when working with ePRO solutions, giving them knowledge of why they hae this device and what they must do with it
- to this end, user-friendliness is vital

The session ended with a discussion around assigning a staff member to work with the logistics of all patient activities, to ensure as much quality data is captured as possible.

REGULATORY AFFAIRS

Roundtables at this year's Regulatory Affairs meeting took place over five tracks, which consisted of: CMC; regulation operations and regulatory strategy; change control; RIM and data management; and labelling.

CHANGE CONTROL

The meeting's change control track began with a roundtable led by Johannes Galatsanos-Dück, Global Head of PLM & Change Control at Novartis, on how integrated product lifecycle management helps to resolve regulatory challenges for product changes.

Here, delegates were split into four groups, each discussing one of a wide range of presented issues within the topic. Some takeaways from this roundtable included:

- A key problem in CMC labelling changes include that no integration exists between systems in different countries: while it is visionary to have a unique, common information platform, such a solution currently does not exist and is not likely in the near future

- When building such a common platform, all groups in he company would have their own requirements for visible information and systems: the platform would need to provide a simple way to access all these for each team - to this end, a common terminology for each "idea" would need to be created to allow full communication

- regarding change control pre-approval, it is very beneficial to formally document and track all changes needing pre-approval to give to inspectors, in order to provide justification for changes made

The track was ended by Youcef Boulemtages, of Pierre Fabre, who aided a discussion on how faster changes can be implemented through post-approval change management protocol.

CMC

The CMC track began the day with an excellent roundtable facilitated by Franz Bucchholzer of Santen, looking at the challenges and experiences in cross-functionally mastering the timely CMC update of a global medical product while considering aspects such as regulatory, financial, marketing, company-strategic, quality and supply. After a break it was followed by another facilitator, Asphalion's André Mota, who discussed how to survive QbD requirements in pharmaceutical development.

After lunch, the track ended with a roundtable by Bayer's Sofia Ribeiro, where delegates discussed procedures and variables in the manufacturing process which must be controlled.

RIM & DATA MANAGEMENT

The session began with Romuald Braun, of Amplexor, leading a roundtable on regulatory information as part of digital transformation. This was followed by another excellent roundtable on shifting to a unified RIM model with one unifying global process and system, led by Thomas Wimmer, Alexion's Senior Manager for Regulatory Information Management (RIM) Lead Global Regulatory Operations.

Some of the key points to come out of this roundtable included:
- While clearly comprehensiveness of datasets is important, equally vital is the means to extract something from said datasets: to this end, ease of use and visibility are needed in this regard
- Free text fields are a major drag on productivity: an ability to sort data and categorise responses is of huge use to industry

LABELLING

The labelling track began with a discussion facilitated by Bayer's Deborah Bebbington, looking at co-ordinating a more robust end-to-end labelling process through CCDS to implementation. That was followed by a discussion from Cecile Riboud, of IQVIA, on labelling management and technologies, and finally Abbott's Anirban Sadhu, who helped delegates discuss effective labelling measures in response to post-marketing safety surveillance.

REGULATORY OPERATIONS REGULATORY STRATEGY

The day's final track began with a roundtable by Takeda's Olivia Maurel looking at the use of real-world data in regulatory decision-making, reflecting on industry experience. This was followed by facilitator Stephan Reynier, talking about achieving quality regulatory operations through outsourcing third-party partners. Some of the takeaways from the session included:

- one outsourcing problem often arises from the pharma company itself, which needs to see evidence of training staff for their records and for legal reasons,
- full benefits of outsourcing regulatory operations are only fully realised when the external body is fully skilled already, a process which will also save money for many companies
- service providers are more cautious with company data than pharma companies often think, because their reputation and future employment are inextricably linked to private, secure services
- Such providers will also refuse to work for any company creating a generic version of a drug they already worked on, no matter how vast the time difference between projects
- Pharma companies differed on the regularity with which they audit and reaudit providers, with some auditing yearly, some less often - but the timescales depend entirely on the task and on evidence submitted of work

KEY DELEGATE CHALLENGES 2020 AND BEYOND

One of the most important resources available to any senior figure in biotech or pharmaceuticals is an understanding not only of the field at present but where the field is going, and the key obstacles that any company in the sector faces.

Proventa International surveyed a number of major players in the field, using expert opinion and insider knowledge to uncover out of the many obstacles on the horizon the major challenges to overcome in the next few years.

PHARMACOVIGILANCE MAJOR CHALLENGES 2020 AND BEYOND

Signal detection
By far the main priority on most delegates' minds was signal detection: identifying safety information from data on adverse reactions. This suggests a heavy focus on better analysing said data, doubtless with new technology and machine learning techniques, over the next few years.

Risk management
Risk management and minimisation were next most important for surveyed delegates. Challenges here related more specifically to implementing electronic methods of minimising risk, and better understanding the effectiveness of risk minimisation measures.

Automation and AI
As with many areas in pharmaceuticals, the desire for greater automation and AI processes in the workplace was crucial to many of those surveyed, with implementation and integration foremost on the minds of several delegates.

Digitalisation and IT
In a similar vein, high on the list of challenges for the future was digitalisation and implementing further IT capacities. Digital innovation in case processing and the need for new digital solutions were particularly mentioned, among other issues.

Hiring and training a team
Another challenge that faced many delegates was the hiring, training and motivating of a workforce: talent acquisition and retention seemed a considerable issue for a number of companies, and will continue to be so for a number of years to come.

PV integration
Integrating pharmacovigilance into a company was another key issue for delegates surveyed, with global-local integration and integrating new products and systems particularly mentioned as key challenges for the coming year.

Medical device regulation and vigilance
Issues around medical device regulation were also mentioned, with specific issues including EU medical device regulations, and questions around whether medical products could find common approval procedures to ease the pre-approval process.

Outsourcing and partnerships
Reducing outsourcing services, determining what can be outsourced to vendors and outsourcing operational tasks all ranked among key challenges for the coming year. Partnerships were also mentioned as of importance, with challenges around partner compliance and on-boarding dogging some companies for the foreseeable future.

QPPVs
QPPVs were the next key issue mentioned by those surveyed. Specific topics mentioned included establishing a QPPV co-operation model with acquired companies, incorporation of global regulations for QPPV requirements and reducing outsourcing services, including the QPPV function.

Document repositories
Finally, delegates surveyed mentioned challenges around document repositories as a probably difficulty in the coming year and beyond.

REGULATORY AFFAIRS MAJOR CHALLENGES 2020 AND BEYOND

Regulatory Strategy
The main challenges facing delegates were, unsurprisingly, related to a broad swathe of regulatory and issues. Specific challenges identified included establishing BPM governance for regulatory, establishing a clear regulatory strategy and guiding its deployment, and the impact of regulatory development on pricing and reimbursement.

RIM
Closely related to the above, the second-largest concern for the coming year voiced by delegates involved regulatory information management (RIM). Surveyed professionals said they were looking for, among other things, end-to-end RIM solutions, better optimisation of processes in alignment with the RIM system, and better selection and implementation of a RIM tool.

Hiring and Training Personnel
Thirdly, the training and hiring of employees with key skill-sets was noted as a challenge for 2020 and beyond. Retaining and developing internal talent, as well as keeping team motivation high, were also mentioned in relation to employees and company workforces.

Innovation
Ensuring faster and wider access to innovation and finding out-of-the-box regulatory innovations were both references by delegates seeking new and effective methods to increase business output.

Integration
Integration of both companies and processes were mentioned by experts as challenges for the year ahead, with several delegates voicing frustration at the process of integrating legacy organisations into a single entity.
Process harmonisation and optimisation

Quality (QMS/SOP)
Another key challenges faced by pharma professionals related to quality standards and procedures, with mention made of transforming quality standards into a digital form, quality reviews and understanding the QMS/SOP landscape.

Compliance
Regulatory compliance was another issue high on a number of lists, with specific mention made of understanding priorities around compliance and ensuring global compliance under constantly-evolving regulations.

Data management (Real-world data)
The next highest challenge faced by pharma professionals related to the management and understanding of data. Specific issues included the increasing dependency on real-world data, big data and data security.

Ensuring processes run as smoothly and effectively as possible is another challenge facing expert delegates in the near future. Particular reference was made to labelling harmonisation, optimising regulatory strategies and optimising resources within a competitive and challenging environment.

CMC
Finally, the issue of Chemistry, Manufacturing, and Controls (CMC) regulatory affairs were specifically brought up as a challenge for the year ahead. Delegates referenced improving CMC processes and better understanding CMC regulation as issues that most require addressing.

A LOOK AHEAD: EXPERT OPINION ON THE FUTURE OF: PHARMACOVIGILANCE

THE FUTURE OF PHARMACOVIGILANCE

Adverse drug reactions make up around 7% of all hospital admissions in the US, with half of these thought to be avoidable. Due to increasing pressures on the pharmacovigilance sector to analyse information more swiftly, report patient reactions more accurately and cover greater areas more efficiently, much must change in the coming years in order to meet targets and ensure as many patients are kept safe as possible.

Issues remain that must first be overcome. Many companies are at present allocating greater spend to processing data rather than analysing it, with the processing of this adverse event data costing more in both money and resource requirements, and becoming less sustainable, with each month that passes.

AI and automatic processing of data are generally seen as the solution to these issues, allowing companies to produce more clear and specific reports of safety problems and intervene more quickly where patient safety is threatened. Such tools will also hopefully encourage greater transparency in the industry, and decreases costs by half.

Global Regulations

He suggested another change to occur in the next five years would be the installation of PV regulations in more regions and countries around the world, possibly also more stringently than they currently are.

He also suggested further requirements for assessing risk management measures outcomes, proving they are actually effective.

Social Media and Proactivity

One facilitator suggested that in the near future the PV sector must become more proactive, with quicker technology matching the ever-increasing needs of patients and health authorities and ensuring the need for swift, on-the-spot decisions and answers.

To find out more about the future of PV, we spoke to some of the expert facilitators at Proventa's Pharmacovigilance strategy meeting, to hear their thoughts on the technologies and processes that will change the field over the next ten years.

AI and Machine Learning

One Director at a major pharmaceutical company echoed industry thought by speculating that AI and machine learning (ML) will be the most important innovations of the next five years, bringing data collection and data entry efficiency gains to the field. These technologies will make signal detection more predictive, using more data sources such as RWE and app data. She noted that humans would still work alongside machines, with new competencies introduced as time goes on.

Another pharmacovigilance head at a leading company seconded this, speculating that there will be a continued focus on big data sources, including social media, and the methods of analysis and reporting.

Social media has a major role to play in this increased proactivity, though Khedr suggests it will never be a totally reliable source of data. That said, it is still a source of insights and information, and mechanisms must be created to filter and capture the right information. None, he points out, currently exist for this purpose.

New Challenges

The pharmacovigilance Head did note that the next few years would still bring more challenges to the table, however. He said as drug developments continues, special adverse events or special types of events, with a greater severity or time of occurrence, would still trouble the PV community. He suggested another issue could well be the increased need for long-term safety data, as new types of drugs come to market.

THE FUTURE OF REGULATORY AFFAIRS

The future of regulatory affairs in the pharma space is also one of considerable challenge and changes. A number of issues prevent the area from operating as efficiently as it could: the necessity of tailoring submissions and plans to local data and regulatory requirements is onerous, while the diversity of public health issues has proven equally challenging. Communication between relevant parties is lacking, and proficiency with new technologies and innovations is slow in coming.

Overall, a number of ideas have been suggested by industry as a means to revolutionise and elevate regulatory affairs as a whole. The idea of global standardisation of regulations for drug products could reduce the cost of individualised data and regulatory requirements considerably, with the ICH mission potentially a huge contribution to this goal. Some have even floated the suggestion of a global regulator, free of cost constraints local agencies suffer under and with pooled resources that could remove bottlenecks and avoid duplication of effort.

Other areas of change have only been speculated on, including the need for regulatory bodies to liaise with all parties, from healthcare providers to payers, to better manage and mediate reimbursement, and the increasing requirement for regulatory bodies to keep up with new innovations and technologies and adapt their requirements accordingly.

Localisation

One Vice President in charge of quality and technology transfer set out how companies are currently adapting to a lack of global harmonisation. She said that in her experience, many companies are starting to address local markets individually, ignoring the complexities of other markets, with more and more bodies beginning to follow this trend. For the patient, however, this means that those in smaller or more complex markets are not receiving the supplies or new technologies that they need.

Digitalisation

According to one facilitator, another coming change is the inevitable move towards digitalisation. While data protection and curation will continue to be a challenge, the increasing digitalisation of regulatory affairs is providing quick returns and immediate responses to questions, benefitting both regulatory authorities and the patients themselves.

This digitalisation is also helping health authorities talk to one another and compare datasets, understanding more swiftly where there are mismatches and providing quicker turnarounds than would otherwise be the case.

Resource Management

One Head of International Regulatory Affairs said that currently a number of discussions are being had around outsourcing and what should be kept internal, as well as how processes are meant to be automated.

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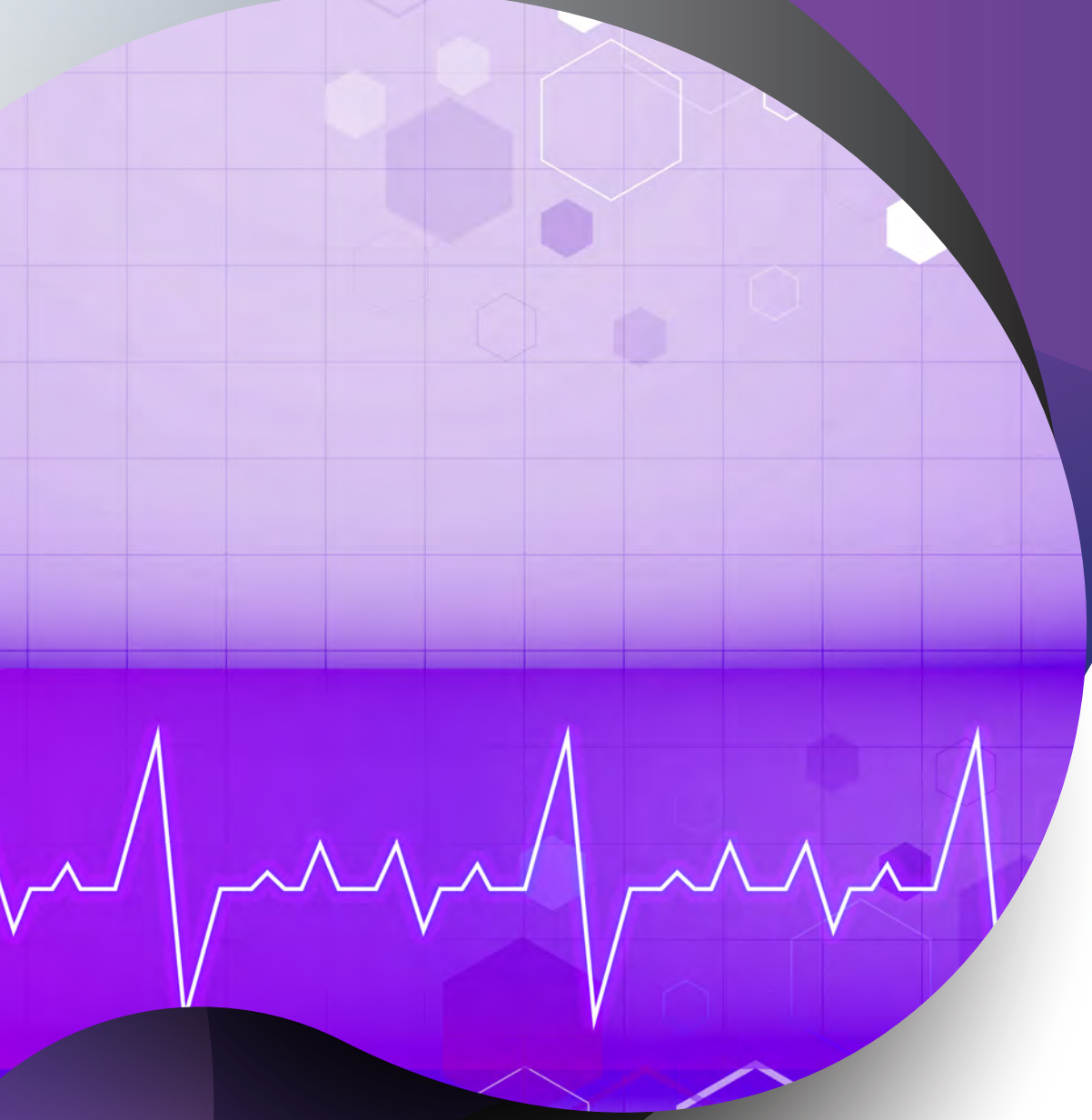

ADDRESS

Ground Floor, Moorfoot House Meridian Gate 221 Marsh Wall
London E14 9FJ United Kingdom

www.proventainternational.com