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COMMENTARY ARTICLE

THE KEYS TO ADDRESSING PHARMA SUPPLY CHAIN CHALLENGES – ESG, DIVERSIFICATION & GLOBAL HARMONIZATION

Since 2022, the global population of > 8 billion human beings have been consuming our natural renewal resources faster and faster, currently at a rate which is twice as much as our planet generates per year. Even commodities such as steel and wood are becoming scarce, as different industries and countries compete for the limited supply. We are also now experiencing the dramatic and often fatal effects of global warming on all continents.

Over the past 30 years, although the global economy has proven that collaboration and innovative technology can solve many problems, as was in the case of Hydrochlorofluorocarbons (HCFCs) becoming a greener alternative to the damaging effects of CFCs, the recent pandemic demonstrated how quickly those improvements can be undermined due to supply chain disruptions such as lock downs, transportation restrictions, and political conflicts. Through this process we have been forced to shine a collective light on the economic responsibilities connecting global warming, the need to consume fewer resources, and shifting supply chains.

Since all these events profoundly affect the pharmaceutical industry as well, we asked 23 CDMO panelists what they consider to be the greatest challenges in maintaining Pharma supply chain continuity. Among the responses, we identified common themes such as the increasing requirements for sustainability, the need for diversification of suppliers and regions, and the additional costs associated with them both as the major fields to be addressed for the Pharma supply chain of the future.

ENVIRONMENTAL, SOCIAL & CORPORATE GOVERNANCE (ESG) REQUIREMENT

The globalization of the world economy has made it very transparent that we all live on the same planet, where environmental pollution and global warming do not stop at national borders. Therefore, governments worldwide have implemented high standards for Environmental, Social, and corporate Governance (ESG) across all industries, including Pharma. Big Pharma companies expect that all companies in the supply chain adhere to the same principles, including their CDMO suppliers. As a result, Europe and the United States initiated several legislative activities from the Task Force on Climate-related Financial Disclosures (TCFD) and the Modern Slavery Act to the incoming US SEC Climate-Risk Disclosures rules.

Ingrid Vande Velde from PCSI points out that investors prefer companies that comply with ESG standards, since non-compliance can represent serious long-term business risks. However, all countries and companies involved in the global pharmaceutical industry should harmonize and develop these standards jointly. Otherwise, economics might drive pharmaceutical production to countries with laxer regulation and control by the authorities, as Paolo Tubertini from Olon Group comments, leading to further concentration of the production capacities in certain regions with lower standards.

Many panelists see the reduction of their carbon footprint as one of the major aspects of ESG. Most CDMOs have already joined an existing initiative such as Science-Based Targets initiative (SBTi) or EcoVadis.

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CordenPharma International - Member of Chemistry Today – Chimica Oggi Scientific Advisory board

Adriano Indolese *studied organic chemistry at the University of Basel, Switzerland and received his PhD from the ETH Zürich for the investigation of Nickel catalyzed cross-coupling reactions in the group of Prof Consiglio. After a postdoc in the group of Prof B. M. Trost at Stanford University, he joined Ciba-Geigy in Basel as a research chemist. He held positions as Head R&D at RohnerChem, Switzerland and Project manager at Siegfried, Switzerland.*

At CordenPharma, he manages the process and analytical development globally in the fields of APIs and Drug Products. His main interest is the improvement of the productivity by new technologies, e.g. Flow Chemistry and Super Critical Fluid Chromatography.

PHARMA SUPPLY CHAIN

source: efcg.cefic.org

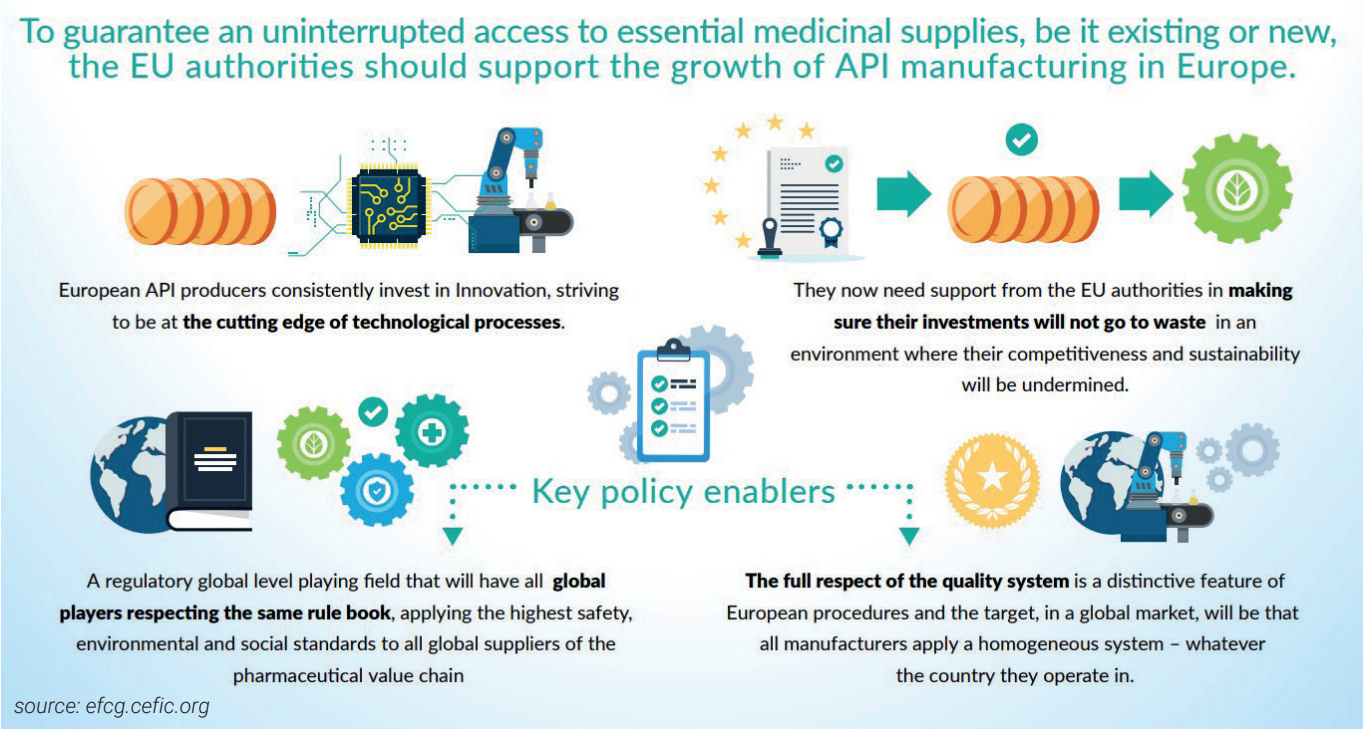
Some companies are developing their own programs. In general, ESG initiatives occur on different levels: 1) They start with energy efficiency projects in the existing plants to reduce energy consumption; 2) They switch to renewable energy sources by installing, for example, photovoltaic panels at the sites; 3) They explore and implement new, more energy-efficient technologies such as Flow Chemistry; and 4) They work with their suppliers to reduce the carbon footprint of the incoming goods.

The first two activities can be implemented quickly with limited investment and clear payback times. The latter two are more challenging, as they also affect the regulatory filing that increases cost and timelines. Many panelists mention the different requirements of the authorities for regulatory changes as a real obstacle for the fast implementation of improved processes or new starting materials. Specifically, greater regulatory scrutiny increases the hurdles for new material qualification, as Stefan Randl of Evonik points out. Herve Bedrou, from Piramal Pharma Solutions, hopes that the regulatory systems can be globally harmonized, leading to convergent international standards and mutual acceptance of data for regulatory filing.

To enforce the new ESG standards, the need for audits will increase. However, since some companies say they are already at the limit of hosting customer and authority audits, Jim Fries of Rx-360 proposes going for joint audits or licensing audit reports by globally accepted auditing companies.

DIVERSIFICATION OF SUPPLIERS & REGIONS

In the past few years, we saw different events that disrupted the pharmaceutical supply chain in unprecedented ways - shutdowns of facilities in China due to environmental problems, the blockage of the Suez channel, Covid-19, and the war in the Ukraine were completely unpredictable factors affecting the pharmaceutical industry as a whole. They not only led to problems and delays in pharmaceutical production, but also shortages of crucial, life-saving medicines, where some countries went so far as to restrict the export of medicines, which only compounded the situation. It's safe to say we all hope governments will prepare better for such events in the future through closer collaboration and more sound science-based decision making, which takes into account that pandemics and the expected effects of global warming such as flooding, storms, and droughts will occur more often.



source: efcg.cefic.org

Many companies act now by applying a multitude of approaches, depending on their expertise and position in the market. This includes diversifying their supplier region, stocking of critical raw materials, and identifying alternate reagent sources, as Michael W. Pennington of AmbioPharm comments. Procos (Chiara Rigotti and Paolo Paisoni) focuses on developing close relationships with carefully chosen preferred suppliers and having several backups for key raw materials in different regions.
Ed Roullard from Actylis, points out that a proper risk mitigation and thorough analysis of the supply chain is key for success. The back-up supply chain must be truly independent, and must not go back to the same intermediate suppliers.
Some companies like Uquita India (Kishore Reddy) consider backward integration and using closer suppliers as a good strategy to make the supply chain more resilient.

Anming Liu, WuXi STA, explains that insourcing could be an opportunity to open new business fields, such as WuXi STA did by developing its own amidite manufacturing capability for their oligo customers, which resulted in them now offering more than 300 types of catalog amidite products to the market.

Europe noticed the painful dependency on India and China for certain medicines during the Covid pandemic. Several panelists mentioned the governmental tender systems in Europe and the US with the sole focus on price as one cause for the concentration of the generics in India and China.

Many countries announced aims to strengthen their pharmaceutical industry, and Chris Neasham, Almac science, thinks that the manufacturing is shifting back to the west. France, for instance, initiated large programs. However, Elizabeth Stampa, President of Medicines for Europe, noticed that beyond these big announcements, so far the initiatives only received minimum support in most European countries. We will see if the European governments have a sincere and sustainable intention to support more robust and diversified pharma supply chains, and to also consider other aspects such as such as sustainability and supply chain security in their public tender systems for medicinal products.

Several panelists, including Matthieu Gobillot, Seqens, expect that India's chemical industry will benefit from the situation, as there is a clear support by the government and a large pool of exquisite talents. However, Chiara Rigotti and Paolo Paisoni, of Procos point out that China will remain more competitive for certain raw materials, due to their lower environmental standards. Both India and China remain big players in the pharmaceutical industry.

INCREASING COSTS & INFLATION

Due to the financial pressures during Covid, coupled with increased energy prices, we now observe a worldwide inflation, which is very pronounced in the EU. Actions to mitigate the supply chain risk and implement ESG principles also increase the production cost in the long-term. Stefan Randl, Evonik Health Care, thinks that the backward integration of regulatory starting materials helps to stay competitive, while ensuring quality and supply security. Dr. Shijie Zhang, Dr. Jack Chen, and Celine Chen say Pharmablock is focusing on upgrading their chemistry - e.g. flow chemistry, micro-packed bad hydrogenation and bio catalysis - in order to reduce carbon footprint, while keeping the cost low.

Kenneth N. Drew, Flamma, comments that for generics, it is very difficult to transfer the additional cost from supply chain disruptions to customers, as in many cases the prices were negotiated before the crisis for very long-term contracts. Andrea Sentimenti of Bormioli points out that where the margins were low before inflation, the increase of energy and raw material cost has caused a dramatic erosion of margins for the generic market. Therefore, authorities should transform the system of public tenders so that buying decisions are not only made on price, but also consider supply security, social and environmental impacts (Ana Marti, Medichem).

Since innovative pharmaceutical companies are more open to accepting higher prices, the chances are better that a part of the inflation and ESG costs will be jointly covered by the CDMOs and their customers. Nevertheless, CDMOs remain under strong pressure to reduce cost and optimize their supply chain.

CONCLUSION

The Pharma industry faces big challenges, not the least of which is that we compete with different industries for the same limited resources. We must fight global warming and deal with its effect, all this in uncertain geo-political situations. As paradigms shift, we probably all agree with Timothy Woodcock of CordenPharma that "the biggest challenge is to adapt our mindset - the way we think and what we will accept - in Supply Chains of tomorrow."

Pharmaceutical companies apply different approaches to cope with the future challenges - including Artificial Intelligence and block chain technology – that can help to make the supply chain more predictable and resilient.

Changing production processes are currently a lengthy and costly endeavour due to the filing of the regulatory changes to different authorities. The health care authorities could further support the transformation of the industry by implementing globally-harmonized procedures for changes and mutually accepted data.

Governments play the most decisive role in the transformation of the Pharma industry, as they can set the proper incentives by implementing the appropriate legislation. These incentives should reward companies that have implemented measures for environmental protection and CO_2 reduction, as well as high ethical standards. The legislation must be globally harmonized; otherwise, companies complying with the higher ethical and environmental standards will be at a continual disadvantage against those that do not have obey the same strict standards. Here, it is crucial that governments and authorities demonstrate their willingness to collaborate openly and peacefully to solve the problems which not only affect the supply of life-saving medications for patients, but also the future of our global community and planet.

PANELISTS

MAGGIE SAYKALI - EFCG, PAC

ELIZABETH STAMPA - President, Medicines for Europe

INGRID VANDE VELDE - Chair of the Pharmaceutical Supply Chain Initiative (PSCI)

JIM FRIES - CEO, RX-360

ED ROULLARD - Senior Vice President of Marketing & Operations, Actylis

CHRIS NEASHAM - Global Procurement Manager, Almac Sciences

THOMAS S. MOODY - VP Technology Development and Commercialisation, Arran Chemical Company, Almac Sciences

MICHAEL W. PENNINGTON - Chief Scientific Officer, AmbioPharm

DENISE KAROUNOS - Sr. Marketing Manager, AmbioPharm

FRANÇOISE DURAND-RIVOIRE - Global Head of ESG, Axplora

NATHALIE FOLTRAN - Purchasing Director, CDMO BU, Axplora

LUIS SOLERA - CEO, Bioiberica

ANDREA SENTIMENTI - Marketing & Innovation Director, Bormioli Pharma

TIM WOODCOCK - Global Procurement Director, CordenPharma International

B VIVEK - Executive Vice President – Global Head of Supply /Planning / Demand and Delivery -PSAI, Dr. Reddy's Laboratories

STEFAN RANDL - Head of Drug Substance, Evonik Health Care

KENNETH N. DREW - VP Flamma USA, Flamma

ANA MARTI - General Counsel, Medichem

PAOLO TUBERTINI - CEO, Olon Group

SHIJIE ZHANG - CTO, PharmaBlock

JACK CHEN - Vice President of CDMO Business, PharmaBlock

CELINE CHEN - Senior Director of Marketing, PharmaBlock

HERVE BERDOU - Chief Operating Officer, Piramal Pharma Solutions

CHIARA RIGOTTI - Purchasing & Sourcing Manager, Procos

PAOLO PAISSONI - BD & Innovation Director, Procos

MATTHIEU GOBILLOT - Supply chain, Procurement & Customer service Director, Seqens

ARVIND SINGH - Executive Director, Global Supply Chain, SK pharmteco

ANIL KANE - Senior director, global technical scientific affairs, pharma services, Thermo Fisher Scientific

PHILLIP LOCKHART - Director, procurement, drugs and pharma, global procurement, Thermo Fisher Scientific

ANMING LIU - Vice President of Technical Operation, WuXi STA

at 360°. Our corporate guidelines provide that we close the collaboration in case of failure to sign. More than the 70% of our global purchases comes from suppliers that have formally accepted and signed the code of conduct.

Actually, we are working with our system that is very well integrated and we are adapting it to make the product traceability easier and increase the effectiveness of our supply chain process management.

Olon is engaged in a series of projects that can revolutionize the supply chain of some industries.

With some of our partners we are reinventing supply chains reaching a level of sustainability never achieved before. We are innovating the processes. I can mention, for example, a new process to obtain animal proteins not using animals but through microbial fermentation technologies. Potentially it can have huge impacts on global sustainability in terms of land and water consumption as well as emissions into the atmosphere.



SHIJIE ZHANG[1], JACK CHEN[2], CELINE CHEN[3]
1. CTO, PharmaBlock
2. Vice President of CDMO Business, PharmaBlock
3. Senior Director of Marketing, PharmaBlock

TECHNOLOGY INNOVATION-EXPLORE A UNIQUE SOLUTION FOR SUSTAINABLE SUPPLY CHAIN

What are in your view the biggest upcoming challenges in supply chain?
Sustainability has evolved as a prominent consideration in pharmaceutical supply-chain management; pharmaceutical and biotech companies' sustainability concerns have expanded beyond the reliability of their raw material suppliers to encompass the challenges of carbon emissions, water usage, and waste. As a critical player in the pharmaceutical supply chain, CDMOs should take proactive responsibility and collaborate with pharmaceutical and biotech companies to develop and adhere to their sustainability targets.

Which strategies do you consider as suitable to mitigate the risks in supply chain management? E.g. re-shoring, back integration, diversifications of suppliers and regions? What are the benefits and risks?
The risks in recent years are very much geo-politically headlined while less is discussed on traditional risks such as economic and environmental changes. A balanced view is needed. For small molecules, the very long supply chain all the way to basic chemicals and reagents has been firmly rooted in Asia, particularly in China over the past 30 years. The entrepreneurship spirit that has been powering the supply chain changes will continue to support the innovators in the west and the increasing innovators in the east. CDMOs that are capable of back integration to the long supply chain, and having strong chemistry capability to make key intermediates and reagents, are preferred partners to mitigate risks. Global footprints give some of them more levers to transfer key materials and/or manufacturing across borders on behalf of clients. Risks will persist, but solutions are being generated. Trusted and capable partners are the best way to mitigate risks.

What initiatives or programs do you consider as appropriate to improve the robustness and resilience of your supply chains in the current environment of increasing political uncertainty and transportation problems due to lockdowns and closed borders? Do you expect to transfer some of the cost to your customers? What initiatives or programs have you initiated in the past 6 months?
Expanding its global footprint is what PharmaBlock has been working on to strengthen the supply chain. We have R&D and production facilities in both China and the United States. In addition to the Process R&D Center in Hatfield, Pennsylvania, our new facility in West Chester, Pennsylvania, will be operated in the coming March to improve clinical API supply capabilities in the United States. We are also seeking chances to expand across Europe.

Furthermore, we have been improving continuous business planning and execution across all the research and manufacturing facilities, and developing multiple backup sources for key materials. Even though local pandemic management in China is rigorous, authorities have gained experience in how to better balance emergency management and normal production and operation.

Costs are growing due to increased energy, transportation, and raw material costs, but passing the cost on to customers is not a long-term solution. We believe that only by fundamentally upgrading chemistry and low-carbon technologies, including but not limited to continuous flow chemistry, micropacked bed hydrogenation, bio-catalysis, etc., can we drive pharmaceutical manufacturing to be more efficient and ecologically friendly, hence reducing the cost.

How could / should governments support the reorganization of the chemical and pharmaceutical industry to help improve the supply security? What technologies should they support?
Continuous flow manufacturing is one of the most efficient solutions to handle green energy challenges and enhance efficiency; combined with automation and digitalization, it will genuinely transform chemical and pharmaceutical production. The ICH guideline has outlined scientific approaches and regulatory considerations specific to the continuous manufacturing of drug substances and drug products. Governments should encourage and push the regional development of this sustainable technology. We have implemented continuous flow chemistry and micropacked bed hydrogenation technologies in both China and the United States, from research to commercial scale.

What action do you have planned to manage the increasing requirements for sustainability and reduction of carbon footprint in your supply chain?
We have invested heavily and will continue to invest in multiple fronts to support sustainable economic development and reduce the carbon footprint in our supply chain. In addition to the current continuous manufacturing workshop equipped in PharmaBlock Zhejiang, a new

workshop dedicated to flow chemistry is planned and to be built in the next two years that will further reduce energy consumption in manufacturing. PharmaBlock's Technology Innovation Center" (TIC) has recently added two groups, chemistry and process, in addition to the three original groups, equipment, flow chemistry, and enzyme/catalyst. The mission of TIC is to invent new technologies to improve manufacturing efficiency and reduce environmental burden such as waste generation. The chemistry and the process groups focus on developing new chemistry to greatly improve chemical synthesis efficiency and reduce PMI, rendering manufacturing greener from the origin. Recently PharmaBlock was honored to receive the 2023 CMO Excellence in Green Chemistry Award presented by ACS GCI PR (ACS Green Chemistry Institute Pharmaceutical Roundtable). The award-winning project was for a novel continuous process for producing an intermediate used in the API synthesis of multiple marketed drugs. The work helps achieve 20-fold efficiency in terms of energy consumption, workspace, and workforce, in addition to much lower PMI.

HERVE BERDOU
Chief operating officer, Piramal Pharma Solutions

SUPPLY CHAIN CHALLENGES IN THE CURRENT GEOPOLITICAL CLIMATE

The current global supply chain for the pharmaceutical industry is at risk due to geopolitical situations, transportation obstacles and production issues. The Zero Covid Policy in China, territorial conflicts like the Russia-Ukraine war, and a potential energy crisis that's facing Europe will lead to short term supply disruptions, inflation, and lower demand. However, in terms of the mid- to long-term outlook, it will give growth momentum to players like India, and they can establish themselves as an alternative to China for raw materials. Developed countries may plan to keep the last steps of their value chain with them while continuing to buy the required raw materials (key chemicals, starting materials, advanced intermediates, APIs) from other countries with an established supply base, such as India. And things are moving fast in India as a result. Thanks to money received from the government and investments in research, India is well positioned to be a strong competitor to China. With all the initiatives put in place by the Indian government and a stable political climate with solid leadership, India is on the right path to become a global production hub, and possibly "the world's pharmacy." Reliable supplies, educated and skilled manpower, no language barriers and an established ecosystem give an edge to India.

Homogenizing the Regulatory System

The regulatory landscape represents its own set of challenges to the pharma supply chain. It is increasingly complex, with new requirements coming into force. The regulators and policymakers should work collaboratively with the industry globally to reduce the burden of disease on patients by providing innovative, safe, and cost-effective drugs. We all need to have a patient-centric mindset. This is only possible through a homogeneous regulatory system. The homogeneity of regulatory systems globally can be realized by developing convergent systems through mutual acceptance of data and internationally harmonized standards. Organizations like ICH, WHO OECD, USFDA, EMA, MHRA, TGA, Health Canada, PMDA have adopted harmonized standards and guidelines, as well as mutual recognition for GxP inspections, thereby reducing the burden of duplicate data generations. Even though much progress has been made over the decades, there are still regulatory gaps that need to be narrowed by effective implementation and collaborations between regulators. There is need to adopt to new technologies and upgrade the skill sets of the people across all stakeholders (regulators, industry) involved in drug development and approvals process. In many developing nations the regulatory systems are still evolving. WHO, ICH, EMA, USFDA are supporting the national agencies of developing nations by providing training to reviewers and assessors to develop skill sets and expertise. These types of engagements between global regulatory agencies are progressing positively to achieve harmonized process, systems, and strategies. However, additional resources are required to have a transparent, technology driven system. Both regulators and the industry are committed to achieve the vision of ICH to have unified harmonized standards for drug development.

There are areas where the regulators need to focus on creating a homogenous system for the classification of changes. Due to different classifications, the timelines for post approval changes varies. This puts a burden on industry from the compliance perspective. To bridge gaps in the regulatory system it is important for all stakeholders (regulatory, industry) to effectively collaborate and to adopt to new technologies. This will create more convergent environment for achieving a homogenous system globally through harmonization, collaboration, common standards, transparency by sharing the data to support timely, risk based, cost effective solutions to patients. The mutual acceptance and data sharing among regulators in developing nations will help to optimize the resources and thereby avoiding drug shortage.

As an organization, Piramal is striving to have uniform processes and systems for quality and regulatory to improve compliance. We are in the process of implementing Regulatory Information Management (RIM) systems to record and track data for compliance purpose. This will help to create a more homogenous system across sites and ensure compliance and support common data sharing across global agencies.

Improving Technology to Streamline Bureaucracy

The gap between the pace at which some companies are adopting breakthrough technologies and their understanding by the regulators remains wide. Regulators must establish processes for rapidly advancing technologies and new treatments, since those used for simpler technologies and small molecules may not work well. High performance computing and simulation is a good example of an area where regulators need to make sure their methods match the sophistication and resources of the tools and approaches being adopted by sponsors.

To serve the need for patient centricity and health care demands, industry is trying to speed up access to treatments around the globe. Global regulations and policy therefore also need to evolve rapidly, as often the rigidity and diversity of the current frameworks do not permit sufficiently nimble and swift responses. Innovation is often slowed by the significant bureaucratic hurdles required for obtaining and maintaining licenses worldwide.