Access to public information has increased exponentially and globally in recent years, steering and influencing the development of various governments’ public policies (1). In the regulatory fields, access to information has distinct characteristics compared with other government sectors because much of it could potentially interfere with the competitive process.

In the field of health regulation, widespread access to clinical trial data is increasingly common in the United States Food and Drug Administration (FDA) (2), European Medicines Agency (EMA) (3), and Latin American agencies. These Health Regulatory Agencies (HRAs) approach the subject from different perspectives since access to data must consider several legal, technical, and ethical aspects, as well as rights safeguarded by various legislative frameworks, i.e., intellectual and industrial property rights, patent rights, commercially confidential information, privacy of research subjects, arrangements and publicity tools, clinical trial registration, e-submission, and delineated access limits (4, 5).

In health surveillance, one of the most important activities for HRAs is controlling the drug production process. The drug lifecycle includes, but is not limited to, development, registration, production, marketing, and monitoring. The registration phase involves the marketing authorization holder espousing the product’s safety and efficacy, which in practice is demonstrated by the clinical trial reports.

Public access to data and information from clinical reports has generated much debate (6, 7). The appeal for transparency is accelerating and has proved to be unavoidable for HRAs (8, 9). In several journals, approval and publication of a paper is now bound to an open-access agreement regarding all reported data (10), and some pharmaceutical companies have established platforms for making clinical data available to the public (11). Despite being positive steps, these approaches arise in a non-systematic way; hence, institutional regulatory transparency policies, as well as tools for arrangements, should be consolidated and coordinated among the major global regulators.

The World Health Organization (WHO) and the Pan American Health Organization (PAHO) have followed the guidelines of the Good Governance Program for Medicines (GGM) (12), which are aimed at preventing corruption in the pharmaceutical sector through transparency and accountability policies, thereby strengthening the health systems of the countries involved. Implementation of the GGM project comprises cooperation among regulatory agencies, civil society, and the regulated sector, as demonstrated in cases such as the Medicine Transparency Alliance (MeTA) (13)

and the Regional Platform on Access and Innovation for Health Technologies (PRAIS) (14), both of which support the principles of regulatory transparency and information sharing, and in turn, fortify HRAs.

From an ethical standpoint, public availability of clinical trial reports would significantly reduce the number of trials performed by different sponsors to obtain the same data. For example, in Brazil about 15% of clinical studies on bioavailability and bioequivalence are pilot projects aimed at obtaining pharmacokinetic data on products that are already available on the market; in other words, obtaining data that is held by HRAs, but not made publicly available (15). Many sponsors do not publish their research results in journals to prevent competitors from gaining access to important information. If and when they do publish, the focus is generally on studies that showed positive results (16). Data relating to about 50% of the new products approved by the FDA are also unpublished (17). Therefore, when implementing public policies on regulatory transparency, whether conservative or enterprising, the regulatory impact on society, governments, and the production sector should be considered, as well as the range of risks and benefits involved in the process.

**DISCUSSION**

The process of regulatory openness represents an evolution in the relationship between HRAs and society. New global approaches to regulatory openness steer towards a common understanding of the need for continuous expansion of transparency and data access. However, such openness must balance the need for protection and promotion of public health with development and biotechnological innovation (18). When performed in a sustainable manner, disclosure of clinical data offers significant benefits to public health (19), especially when it strengthens the decision-making process (20).

In society, access to information offers patients a better understanding of the risks and benefits of prescribed treatments. Everyone has the right to know the circumstances under which their medication was approved or produced; indeed, this information is essential to choosing the treatment best suited to an individual’s needs. Similarly, healthcare professionals, especially prescribers, should be integrated into the registration process; in particular, they need access to safety- and efficacy-related evidence. For regulators, who typically have a limited amount of time for decision-making, transparency that includes the sharing of the technical rationale for the approval/disapproval of health products and services demonstrates an HRA commitment to public health safety.

For academics, a source of complete information is important for new investigations, reanalysis, and meta-analysis, and it enriches the quality of health research. Meta-analyses can identify risk associations and demonstrate the idiosyncrasies of certain products; however, the robustness of these analyses is directly related to the quality of the original data (21, 22). Furthermore, re-analysis can be used as a source of external accountability, capable of revealing the flaws in methods and discouraging the adoption of technically fragile or questionable practices (23).

Approval of a product without robust guarantees of safety or efficacy can lead to increased health care costs: first, costs are incurred for ineffective treatment; and second, re-treatment can be even more costly because the untreated disease usually tends to worsen. More dangerous and expensive than ineffective products are products that cause harm. These lead to additional treatment costs, as well as the expense of legal repercussion and remediation.

Proactive transparency tends to restore consumer confidence in pharmaceutical and research companies, a confidence that has been previously shaken by numerous lawsuits and recalls originating from issues of inefficiency, false claims, and omission of adverse events (24). Additionally, the billions spent on fines and lawsuits could instead be applied to research and new product development (25). In this respect, many large companies have decided to advance the global trend of regulatory openness by independently disclosing all clinical studies after obtaining regulatory approval (26).

Publishing safety and efficacy data from clinical trial reports tends to lower the global cost of drug research and production, as well as potentially increase the development of treatments for rare diseases with expansion to clinical trials. Thus, the outcome of research and development becomes more effective, reliable, and feasible. Many pharmaceutical products are manufactured or distributed by single owners, and are more apt to be in short supply, mainly due to the loss of marketing authorization resulting from quality infractions, or even, disinterest. New manufacturers are then required to “redevelop” the complex knowledge related to an old product’s pharmacokinetics, pharmacodynamics, and safety and efficacy profile; however, this knowledge already exists in the archived files of previous owners, but it is not publically available yet. Medicine shortages, lack of treatment for rare diseases, and the high cost of treatment are all harmful to public health, highlighting the responsibility of governments and HRAs to produce policies and regulations that mitigate such events or patterns.

There are countless benefits of widespread transparency in regulatory systems; however, some pharmaceutical conglomerates still oppose and resist new approaches for data access and disclosure, openness policies, and regulatory transparency (24). For the pharmaceutical industry, broad dissemination of clinical trial data may result in violation of research subjects’ privacy, as well as the loss of intellectual property rights and commercial secrets (27).
In contrast to the promotion of public scrutiny, inconsistent re-analysis or assessment without adequate methodological rigor can spread outcomes that are untrue, and that greatly undermine public health policies, thereby jeopardizing the current regulatory system (28). This is the case with certain vaccination platforms, which are often affected by rumors of ineffectiveness or harmfulness. From another perspective, inappropriate re-analysis may still be linked to disclosure and publication of poor or biased data, a claim that strengthens the need for increased access (22).

It is a regulator’s duty to protect commercially-sensitive data, as well as research subject’s privacy. However, in some cases there may be “overriding public interest,” meaning that the general public’s wellbeing is deemed to outweigh the confidentiality of commercial interests (29). In addition to public health issues, the individual’s right to health should receive the proper attention of policymakers (30). Conceptualizing and defining the limits of access to this kind of data are perhaps the main challenges for policymakers and governments that support regulatory openness.

In regards to technical requirements, data disclosure should involve up-to-date technologies and free access formats, and it should occur proactively within a reasonable time, i.e., prior to requirements, with data that is easily searchable and downloadable (31).

The quality of the disclosed information is also an important element in the process of regulatory openness. Quality is related to the integrity, objectivity, and usefulness of the content, with the latter characteristic focused on accurate, direct, complete, reliable, and unbiased presentation (32).

Some clinical trial platforms seek to provide information that is complete, valid, and user-friendly (33). Good examples are those of WHO (International Clinical Trials Registry Platform [ICTRP]); the FDA (ClinicalTrials.gov); the European Community (European Union Drug Regulating Authorities Clinical Trials [EudraCT])); and of Brazil (Brazilian Register of Clinical Trials [REBEC]) (34).

The improvement of technical arrangements is essential for achieving a regulatory openness policy, and necessary for improving health surveillance. In particular, registration systems and computerized databases with a standardized language, capable of adapting to different audiences (from a layman citizen to a researcher) in a prompt and agile manner, will be fundamental to a robust and consistent policy of openness.

PERSPECTIVES

The United States FDA is at the forefront of incorporating open data as a pillar of modern regulation. With direction from President Barak Obama, the FDA launched a public transparency program that gained momentum with the consolidation of the Open Government project (35). This project expresses the United States Government’s commitment to ensuring an “unprecedented” level of openness, with the aim of increasing public confidence and participation, strengthening democratic systems, and promoting the efficiency and effectiveness of government actions (35). The Open Government project is part of the political agenda of many countries, some of which are in Latin America.

The European Community has jointly built a robust framework of regulatory transparency with the FDA. In October 2014, EMA decided to publish clinical reports that underpin decision-making regarding medicine marketing authorization. This landmark policy came into force on 1 January 2015, and from that point forward, data began to be proactively disclosed. In contrast to previous approaches, the new policy seeks to make available all of the data in clinical trial reports, a change that will significantly influence the pharmaceutical regulatory environment (3).

In Latin America, these Regional Reference Authorities (RRAs) stand out in terms of regulatory transparency: Brazilian Health Surveillance Agency, Brazil; National Administration of Drugs, Food, and Medical Technology, Argentina; State Control of Drugs and Medical Devices, Cuba; National Institute of Food and Drug Surveillance, Colombia; and Federal Commission for Protection against Health Risks, Mexico (36). The RRAs have quality standards recognized by WHO; and they aim to establish a continuous and perennial flow of information through civil society, academia, and industry, as well as among the regulatory institutions in the Americas. This allows countries with less capacity and poor regulatory frameworks to fall within the global context of open regulation, and thereby improves their decision-making processes.

Among the RRAs, only Cuba does not have a “Right To Information” (RTI) law. Despite the RTI laws in the other countries, none of the RRAs has guidelines or rules aimed at disclosing clinical trial data. Despite the high level of transparency in some member countries, individual approaches to regulatory openness have shown low effectiveness. This may be the result of the pharmaceutical industry’s influence over policymakers. Currently, just EMA has implemented procedures to disclose clinical trial data (3, 30, 37).

Following the global trend on regulatory transparency, RRAs aim to establish and coordinate procedures and approaches that include, but are not limited to:

(a) Establishing consistent guidelines and standards to redact and de-identify personal or confidential commercial data on regulatory dossiers and clinical trial reports.

(b) Making the approval of products contingent on registering their clinical trials on a publically available, international platform, such as the ICTRP.

(c) Adopting public policies that support regulatory transparency.

(d) Defining technological standards (open source formats) for electronic data submission.
(e) Strengthening alliances and Regional platforms established by PAHO/WHO for information sharing, e.g., PRAIS and MeTA.

(f) Defining criteria and adopting measures to proactively publicize information on HRA websites, e.g., smart search tools with download options and regular activity reports.

(g) Aligning concepts with intellectual and commercial property rights in regulatory reports.

(h) Setting the minimum amount of data to be shared publically.

(i) Involving all key stakeholders in developing an open regulatory policy (academics, prescribers, regulators, industry, and civil society).

CONCLUSIONS

The key HRAs in the world are at an advanced stage of implementing transparency policies to improve the quality of public health, having broken many barriers set by the lobbies of some pharmaceutical conglomerates. Moving forward, the public openness approach must be extensive and unconditional, always protecting (through de-identification/redaction) the confidentiality of research subjects, as well commercially-confidential or patent-protected information, except if there is overriding public interest.

Access restrictions no longer hold up against the societal benefits of an open regulatory environment. The claim that regulatory openness may embarrass regulators by exposing errors or failures, as well as increased speculation fears, should not be tolerated. The adoption of good regulatory practices improves the quality of transparency. The guarantee of full and unrestricted access to clinical trial reports may support democratization of knowledge and encourage more citizen involvement, perhaps even society as a whole, in the regulation of the pharmaceutical market. This social accountability may reduce knowledge asymmetry, which until now has been maintained under the cloak of commercial-confidentiality protection. Allowing access to data, however, is just one branch of social accountability. It has to be supplemented by promotion efforts and foment strategies to fully and actively engage civil society.

Dialogues and multilateral initiatives, when well established among the HRAs, will lead to enhanced cooperation and regulatory convergence actions, and ultimately, a transparency policy that is well systematized and harmonized. A robust regulatory transparency policy will, in turn, produce a safe and reliable regulatory environment that protects and promotes the public’s health and fosters products and services that are safe, of high quality, and equitably used.

Conflict of interests. Varley Dias Sousa is a senior auditor at the Brazilian Health Surveillance Agency; however, the views expressed in this paper are solely those of the authors and do not reflect the Agency’s opinion.

SINOPSIS

Transparencia reglamentaria: aspectos sociales, técnicos y éticos del acceso a los datos de los ensayos clínicos

En el campo de la reglamentación sanitaria, la habilitación del acceso público a los datos de los ensayos clínicos constituye un proceso actualmente en fase de consolidación por parte de los principales reguladores a escala mundial. Este artículo trata sobre los recientes avances en las políticas públicas con respecto a la transparencia reglamentaria, y los riesgos y beneficios de un análisis reglamentario de la repercusión en los informes de los ensayos clínicos desde la perspectiva de los interesados directos clave (es decir, los pacientes, los prescriptores, el gobierno, la sociedad, la industria y los organismos reguladores). Por otra parte, se destacan los aspectos sociales, técnicos y éticos del proceso del uso compartido de datos, incluidos los límites de acceso, los datos comercialmente confidenciales y los derechos de patente, la privacidad de los sujetos sometidos a investigación, los acuerdos y las herramientas publicitarias, y el registro de los ensayos clínicos. Además, se muestran las perspectivas en materia de mejora y ampliación de las políticas de transparencia reglamentaria, contextualizando las experiencias norteamericanas, latinoamericanas y europeas, y destacando la cooperación interinstitucional y las iniciativas de colaboración dirigidas a la armonización de los programas de salud y a la convergencia reglamentaria.

Palabras clave: ensayos clínicos como asunto; revelación; confidencialidad; privacidad; acceso a la información; política de salud.

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