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We are today facing the paradox of unprecedented progress in medical science, whilst at the same time seeing the universality of pharmaceutical assistance threatened by the costs of innovation. Striking a balance between the needs of the parties involved in this standoff is not easy: to remunerate the industry's investment in research and development, while granting patients timely access to innovative treatments and containing costs for public healthcare services would seem a daunting task to any EU Member State, especially in times of austerity. To find a compromise between these, often conflicting, needs is the task of the healthcare products Regulatory Agencies: a position as strategically critical as it must be uncomfortable.

Well aware of this is Guido Rasi, Director of the European Medicines Agency (EMA), and before that of the Italian Medicines Agency (AIFA), who from the AIFA's practices draws the conclusion that a solution for the strategic dilemma lies in the improvement of Health Technology Assessment (HTA). That is to say, the assessment of comparative effectiveness of new medicines, which allows one to determine their degree of innovativeness and to fix or negotiate their price on an objective and verifiable basis. AIFA is unique amongst its European counterparts to combine risk-benefit assessment, which is conducted during the registration procedure of a drug, and cost-effective assessment, which is crucial to properly rewarding pharmaceutical innovation.

Italy is on the cutting edge in this combined approach. As a Member of the European Network for HTA, AIFA contributed in 2010 to a cooperation with EMA in promoting the use of the scientific conclusions reached by EMA on the risks and benefits of new medicines in the comparative effectiveness assessment conducted by national Authorities. An initiative, which Mr. Rasi undoubtedly knows how to take forward, due to his wealth of experience gained in Italy.

*Mariella Palazzolo*

Telos is a member of the FIPRA network

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# DIALOGUE ON PHARMACEUTICAL INNOVATION WILL BEAR FRUIT

*"The EMA is aware that the mere definition of the benefit-risk index of a medicine may result in a serious shortcoming over time. The subsequent assessment of its comparative effectiveness might cause a double damage: to patients for their access to treatment, and to the industry for the uncertainty over the timing of market entry."*

**Telos:** You were the Director of the Italian Medicines Agency (AIFA) throughout most of the economic crisis so far, during times when tough negotiations occurred between the different levels of Government dealing with the management of public healthcare spending. How has this climate affected AIFA?

**Guido Rasi:** When I took office in 2008, AIFA was a recently-established agency with great potential but facing several critical issues from both the organisational and structural point of view: this led to a huge amount of outstanding files. We deemed it necessary to draw up a new Regulation of the Agency, which was approved in 2009 and has completely reshaped its structure, allowing it to meet its efficiency and effectiveness targets. As a consequence, AIFA was able to attain a number of important achievements in a short time. For instance, the issuance of Free Sale Certificates, which are the drivers of the Italian export, previously required a non-computerised procedure lasting more than a year and involving several offices; over time we cleared all the backlog and currently it takes only one month to issue a Free Sale Certificate. Moreover, the staff was increased, although it still does not meet the Agency's needs. Considerable emphasis was given to the development of international relations, that allowed AIFA to play a key role in strategic decision-making processes at the European level and beyond. In fact, the Agency strengthened its presence in the international scenario over the last years, both through its participation in International Committees and by signing important Agreements, above all the one with the FDA.
Also, AIFA became a point of reference globally for its solid expertise in the Health Technology Assessment: in fact, it's the only national regulatory Agency which combines the evaluation of the benefit-risk profile of drugs with the cost-effectiveness one.

Criteria and procedures for the assessment of pharmaceutical innovation affect both the remuneration of medical researchers and the patients' access to innovative treatment. As new EMA Director, how do you think that the dialogue between the EMA and National Authorities in

Guido Rasi is the Executive Director of the European Medicines Agency (EMA), where he took charge in November 2011, after serving as Director General of the Italian Medicines Agency (AIFA) from 2008 to 2011. Previously, he worked from 1990 to 2008 in research at the Institute for Experimental Medicine of the National Research Council in Rome, directing the molecular medicine section from 2002 to 2005 and the Tor Vegata section from 2005 to 2008. He was made full professor of microbiology at the University of Rome Tor Vegata in 2008. Rasi is a Medical Doctor with specialisation in internal medicine, allergology and clinical immunology from the University of Rome. His research activities have primarily focused on oncology and chronic viral diseases. He has been responsible of several scientific projects with national and international institutions, such as the National Institute for Health, George Mason University and UC Berkeley. He is author of more than 100 scientific publications.
Born in Padua, he is married with two children. In his youth, he was a professional water polo player, taking part in the 1972 Olympic Games.

charge of HTA will develop in the future?

The EMA is well aware that the mere definition of the benefit-risk index of a medicine may result in a serious shortcoming over time. In fact, the subsequent assessment of its comparative effectiveness might cause a double damage: to patients, in terms of access to treatment, and to the industry, in terms of uncertainty over the actual timing of market entry. In light of the above, the EMA started a collaboration with a European Health Technology Assessment Network, jointly conducting the Scientific Advice and promoting other specific projects such as the revision of the European Public Assessment Reports (EPARs). The dialogue is going on, with very encouraging results, and I am sure it will be fruitful.

The debate on the complexity and length of the authorization procedures for new medicines reveals tension between two objectives: on the one hand simplifying the bureaucratic procedure, and on the other hand ensuring that safe and effective products are marketed to patients. Does the current regulatory framework provide a good balance or do you think that it needs to be reviewed?

The American and the European systems are basically aligned and they have reached a satisfactory level of overall efficiency. Significant room for a change will only be available when the new business model towards which the industry is moving will be sufficiently clear. At the same time, we are assessing new feasible regulatory approaches that include the definition of surrogate endpoints and post-marketing studies. The change in Pharmacovigilance is disclosing new opportunities to EMA which, together with the MIT, Massachusetts Institute of Technology, is developing a new algorithm for the benefit-risk assessment.

The entry of counterfeit medicines into the European Market, particularly from Asia, is regarded as a crucial issue in Italy, as well as in the rest of Europe. Do you think there is any room for cooperation between the EMA and its Chinese counterpart, the SFDA, in the fight to prevent this problem?

Pharmaceutical counterfeiting is a very important issue, whose proportions have turned it into a major worldwide healthcare problem, which also produces a huge economic damage. Counterfeit medicines are dangerous products, packaged like medicines and labeled misleadingly with respect to their ingredients and origin. They share low and non-verifiable quality.
Their spreading is constantly rising, especially due to the opening of global markets and the role played by the Internet, used as a large scale marketing channel by the organised crime. The EMA is enhancing its action to contrast counterfeiting, first of all by closely cooperating with the European Commission and National Authorities for the implementation of the Directive 2011/62/EU and secondly, through international cooperation in other fields, involving, for example, the European Directorate for the Quality of Medicines (EDQM) and the World Health Organisation, as witnessed, for example, by the support that the latter gave to the IMPACT task-force in 2006. Other instruments that were put in place are the Medicrime Convention and the OECD project on counterfeiting and piracy. China is among the main centres for production and distribution of illegal medicines. In fact several types of medicines made in China were seized in recent years: from antitubercular to antimalarial drugs and impotence products. Chinese authorities are putting effort on several fronts in order to stem this phenomenon. In July, a meeting between representatives of the EMA and the SFDA will take place and counterfeiting will no doubt be an important subject for debate.


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