Interview with Daniel Boda, President, National Agency for Medicines and Medical Devices (NAMMD) of Romania

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Tags: National Agency for Medicines and Medical Devices (NAMMD) of Romania

Under various former names for over five decades, the Agency has undoubtedly played a key role in setting a regulatory framework for Romania's pharmaceutical market. Over these five decades, thorough changes in the political regime, subsequent regulatory changes, the emergence of new institutions, and many other factors have drastically changed the landscape of the pharmaceutical market in the country. What have been the key milestones that really shaped – and advanced – the regulatory framework of Romania's pharmaceutical market?

For over 50 years, the present Agency has represented the drug regulatory authority in Romania. Known as the Institute for Medicinal Product Control and Pharmaceutical Research on its setup in 1956, the name of the institution was further changed in 1960 to become the Institute for the State Control of Medicinal Products and Pharmaceutical Research (ICSMCF). Between 1999-2010, by reorganisation of the former ICSMCF, the institution operated as the National Medicines Agency.

The National Medicines Agency (NMA) has continued the ICSMCF tradition in regulation and control of medicinal product quality in Romania. Establishment of the NMA did not occur for reasons of an institutional scientific or professional void, but out of a change in philosophy, which was closer to that of its EU institutional counterparts, involving significant transformation of vision and principles, occurring gradually within a process of connection to European vision and practice in the field. The decisive factor for the evolution of the NMA since 1999 has been the adoption of defined benchmarks, meant for constant guidance of its policies and practice: European landmarks

and primarily those of the then newly established European Medicines Agency (EMEA, currently the EMA).

On 01.01.2000, based on provisions of Order of the Minister of Health no. 802/1999, the NMA structure also included the Centre for the State Control of Biological Products for Human Use, which meant further undertaking by the Agency of the role of Romanian competent authority for biological products for human use and brought about additional tasks as well as an extended stakeholders range.

Main NMA professional activities have been carried on by the NAMMD:

– marketing autorisation and related activities (approval of variations as well as clinical trials, advertising material, pharmacovigilance, direct communications to healthcare professionals on medicinal products)
– medicinal product quality control
– pharmaceutical inspection activity
– regulatory work under the Ministry of Health coordination
– Pharmacopoeia related activities
– quality management activities.

Before Accession to the EU in 2007, the NMA had 26 active observers in EMEA scientific committees and working groups, the most effective means allowing the National Agency to preserve its connectedness with European activities in the medicinal product field.

Through Romania’s accession in 2003 to the Convention on the elaboration of the European Pharmacopoeia, the quality standards of the latter have become mandatory for all raw and starting materials and medicinal products both manufactured in Romania and imported ones.
In June 2006 Romania emerged on the EudraNet map, as result of the NMA successfully connecting to the network of European drug competent authorities in medicinal products for human and veterinary use, under EMEA permanent coordination and monitoring.

The NAMMD is a public institution under the Ministry of Health supervision, founded by Government Emergency Ordinance No. 72 of 30 June 2010 on reorganisation of certain healthcare facilities and amendment of certain regulatory provisions in the healthcare field, due to the merger of the National Medicines Agency (NMA) with the Technical Office for Medical Devices (TOMD). NAMMD organisation and operation were approved by Government Decision nr.734 of 21 July 2010. As shown in the text of Government Emergency Ordinance No. 72/30 June 2010 itself, the grounds for the NAMMD foundation was increased efficiency of healthcare institutions in line with Government priorities for public administration reform, establishment of economic and financial measures for budget funded institutions under the Ministry of Health supervision, in result of the

severe economic recession. The consequence has been addition to the Agency's mission of new obligations related to the field of medical devices.

Through its specialists appointed as members, the NAMMD currently actively participates in committee meetings and scientific working groups of the EMA and other bodies in the medicinal product field. This is the most effective means for the National Agency to make effective contribution to the good progress of European activities in the field of medicinal products for human use.

The activity related to medical devices was set up 50 years ago as well.

As early as 1958, the technical directorate of the Ministry of Health set up its own laboratory for technical testing of medical equipment, which became a distinct entity in 1973 within the Station for Verification and Maintenance of Medical Devices (SVMMD). As of 1 February 2005, the SVMMD has been reorganised under the name of the Technical Office for Medical Devices (TOMD), which in its turn merged with the National Medicines Agency (NMA) in 2010.

As far as medical devices are concerned, the NAMMD is in charge of control of the performance and security of medical devices in use as well as assessment of the capability of organisations providing services in this area.

NAMMD issues an organisational strategy in the context of the legal framework establishing the relation between the NAMMD and the Ministry of Health, as well as between the NAMMD and its stakeholders. It covers a 5-year period and is updated every year.

An important area of concern for all regulators worldwide, remains to be the counterfeit medicines. As supply chains have become increasingly international and as the sales of medicines through new media such as the internet have become increasingly popular, the challenges for regulatory agencies have inevitably been changing. If we compare the current situation to roughly one decade ago, do you see this battle as more challenging? What measures can be taken to align policy with the international community?

As the competent authority in the field of medicinal products for human use, the NAMMD has fully taken up its important role in combating medicine counterfeiting and illegal medicinal product trade and has continued in recent years to inform and warn the public as well as develop collaboration relationships with other institutions and bodies involved in this activity. In that respect, the NAMMD has continued collaboration with national institutions involved in combating counterfeit medicines sales over the Internet, as well as with their institutional counterparts in EU Member States or outside the Community, to limit these criminal phenomena, which sometimes can have serious consequences on public health. For permanent information of the public thereof, in 2010 as well work continued for update of the 'Counterfeiting' heading on the Agency website, reporting

counterfeit information transmitted through the rapid alert system.

NAMMD specialists appointed to attend meetings of the EU Council Working Group for medicines and medical devices have in recent years expressed and supported Romania's views on two draft directives amending Directive 2001/83/EC establishing a Community code on medicinal products for human use, envisaging both avoidance of penetration of counterfeit medicines into the authorised distribution chain and pharmacovigilance issues.

To the best of our knowledge, there are no counterfeit medicines in the legal authorised network for distribution of medicinal products for human use in Romania. Medicines with falsified source, identity or history only penetrate our country via online medicine trading.

As in other countries, the main counterfeit medicines are those for treatment of erectile dysfunction, weight loss medications, or antibiotics, purchased over the Internet or on the black market. According to the Anti-Counterfeiting Association (REACT Romania), Viagra, used to treat erectile dysfunction, is the most commonly counterfeited medicinal product in Romania.

The Agency performs an anti-medicine counterfeiting and illegal trading activities, for information and warning of the public as well as for development of collaborative relationships with other institutions and bodies involved in this activity. Thus:

– For better information of the public, a new 'Counterfeiting' heading was established on the NAMMD website in 2010, including counterfeit reports coming through the rapid alert system.
– In 2009, the NMA initiated and completed a protocol regarding collaboration with the Directorate for Organised Crime and Terrorism Investigation (DIICOT) to combat drug counterfeiting and their illegal trading.
– The Agency has appointed a representative to meetings of working groups on combating counterfeiting, set up by the European bodies in the field, on which occasion the appointed NAMMD representative presented and supported Romania's views in that respect.

Selling medicines over the Internet is prohibited in our country. The measure has been appreciated by the Pharmacists Employers' Association in Romania. Medicines traded over the Internet are not safe, 30% of them being counterfeit, according to some studies, whereas according to the World Health Organization, more than 50% of medicinal products sold over the Internet are counterfeit. While pharmacies in Romania are now prohibited from selling medicinal products over the Internet, online pharmacies are legal in other European countries, within a well-defined national framework.

European Parliament members have considered it necessary to regulate sales of pharmaceuticals over the Internet, which is one of the main routes for counterfeit medicinal products entering the European market. All licensed online pharmacies will be provided with a link to a central site in each Member State and will be listed on that respective website. In turn, the various national

websites will provide a link to a European website. At the same time, citizens will have to be informed on the risks involved in buying medicinal products online.

The first meeting of the NAMMD management with mechanisms involved in establishment of the Romanian legal framework for product traceability, occurred in December 2010; it was a meeting aiming at identification of all elements as possible starting points for viable solutions for its set up.

On June 8, 2011, after years of intense debate, the European Parliament and the Council adopted DIRECTIVE 2011/62/EU amending Directive 2001/83/EC establishing a Community code on medicinal products for human use with regard to prevention of counterfeit medicinal product penetrating the legal supply chain.

The new Directive provides for measures to be implemented by Member States to ensure increased and effective coordination on international level to warrant effective strategies to combat counterfeiting, particularly in terms of medicines sales over the Internet. As shown even in the Directive itself, the Commission and the Member States should cooperate closely and support ongoing work in international fora on this subject, such as the Council of Europe, Europol and the United Nations. In addition, the Commission, working closely with Member States, should cooperate with the competent authorities of third countries with a view to effectively combating the trade in falsified medicinal products at a global level.

The Directive requires EU Member States to implement laws, regulations and administrative provisions necessary for compliance before January 2, 2013, the date for Member States enforcement of those provisions.

While some of the multinational pharmaceutical companies have been actively conducting clinical research in Romania, there is still a vast potential to ramp up an untapped clinical trial potential. Having the right regulatory framework is therefore not only important to attract such activity to the country, it is further imperative to ensure patient safety in the first place. How does NAMMD provide a framework for clinical trials that strikes the balance between patient safety and a smooth authorization process for the industry? What will the further harmonisation with the EU directive on clinical trials bring to Romania?

Member States, Romania included, are known to have drafted legislative proposals related to a Regulation/Directive for amendment of the Clinical Trials Directive – Directive 2001/20/EC of the European Parliament and the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. This proved necessary because of the Community context created by the significant criticism mainly with regard to the varying manner of transposition of the Directive in the different Member States, involving increased administrative load and discrepancy between legal provisions in the field and the global

rising tendency of clinical trials.

To briefly outline proposals for current provisions amendment, the need should be highlighted of the following:

– More efficient/simplification of the clinical trial authorisation procedure through joint assessment of applications for authorisation;
– Clarification of certain provisions of the current Directive;
– Adoption of the new legal provisions as a Regulation – directly applicable into national legislation and not as a Directive, in order to avoid differences in transposition manner on national level;
– Revision of application guidelines;
– Voluntary cooperation for resolution of difficulties encountered.

New regulations have the following goals:

1. Ensuring an up-to-date regulatory frame that takes into account multi-national research and needs of a highly innovative pharmaceutical sector based on research, providing support mainly to the process regarding assessment and follow-up of clinical trial applications against a multinational background;
2. Adapting to practical needs, constraints and needs without compromising the safety, well-being and rights of clinical trial participants;
3. Ensuring a global character to clinical trials for harmonisation on world level, at the same time complying with good clinical practice regulations.

Analysis of the national context results in the following conclusions:

1. Romanian legislation transposes all clinical trial-related directives (as orders of the minister of health) and the greatest majority of European guidelines existent in volume 10 of the EudraLex (as Decisions of the NMA/NAMMD Scientific Council)
2. From the standpoint of social-economical implications, the following are expressly necessary:

o Improving safeguard of clinical trial participants' safety, well-being and rights;
o Reducing costs and administrative load for sponsors and investigators;
o Facilitating clinical research on medicinal products, particularly with regard to multinational clinical trials involving disorders of reduced incidence (e.g. rare diseases) for which additional research is essential;
o Strengthening clinical trial reliability globally.

3. As far as legislative implications are concerned, the need arises for further amendment of orders of the minister of health and decisions of the NAMMD Scientific Council resulting from amendment of Directive 2001/20/EC.

Romania’s preliminary position has resided in:

– Clarification and improvement of definitions provided in the current version of the Directive (e.g. regarding non-interventional studies, investigational medicinal products etc.);
– Simplification and harmonisation of the procedure related to reporting of serious unexpected adverse reactions in clinical trials;
– Clarification and update of labelling requirements for all categories of investigational medicinal products;
– Classification based on clear criteria of clinical trial phases;
– Contribution with clarifications on documents required for special medicinal products (genetically modified medicines, radiopharmaceuticals, advanced therapies medicinal products);
– Additional clarification on terms in the application form for clinical trial approval.

Romania’s regulatory and harmonisation perspectives in the clinical trial field are focused on:

– Transposition/translation and adaptation of European provisions in the field (as orders of the minister of health/Decisions of the NMA/NAMMD Scientific Council);
– Ongoing use of the updated version of the European Clinical Trial Database-EudraCT (in line with the current version of the Directive)
Improving use of the EudraCT through participation in meetings of the EudraCT TIG (Technical Implementation Group)
– NAMMD assigned representatives’ participation in meetings of the Clinical Trials Facilitation Group (CTFG) (starting as early as 2008), a Heads of Medicines Agencies-HMA working group, established for coordination of Directive 2001/20/EC implementation in all Member States on national level;

o Within the CTFG, a procedure has been established for harmonised assessment of multinational clinical trials: the Voluntary Harmonization Procedure-VHP, running for two years now and still in its pilot stage, also involving Romania from the very start;
o VHP goal is focusing clinical trial assessment on subject safety as well as on quality and safety of investigational medicinal products.

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