

HOW LONG IS THE ARM OF BIG PHARMA?

Corinne Hinlopen (Global health policy researcher)

How does the pharmaceutical industry influence the European Medicines Agency? Can the organization operate independently? On January 9th, experts discussed these and related questions in the European Parliament. With this event, organized by Wemos and the European Parliament group of SP (GUE/NGL), we aimed to call on the European Medicines Agency (EMA) and the European Commission to consider the added therapeutic value of new medicines before issuing marketing authorization, and to strive for more independent clinical research.

The discussions took place before an impressive audience of some 100 interested persons from different walks of life, e.g. political parties, patient advocates, health interest groups, pharmaceutical associations, and journalists. There were two expert panels: the first included experts from European institutions - Martin Seychell (Deputy Director in Directorate-General Health of the European Commission), Noel Wathion (Deputy Executive Director of the EMA), and Fergal O' Regan (Head of Inquiry Coordination at the European Ombudsman). The second panel consisted of Dick Bijl (president of the International Society of Drug Bulletins (ISDB), former general practitioner and former editor-in-chief of the Dutch Drug Bulletin), who spoke on behalf of Wemos, Yannis Natsis (Policy Manager Universal Access and Affordable Medicines at European Public Health Alliance), and Silvio Garattini (Director of the Mario Negri Institute for Pharmacological Research).

Conflicts of interest in all sectors

Dennis de Jong (Member of European Parliament (MEP)) hosted the panel discussions. MEP **Bart Staes**, rapporteur for the agencies on behalf of the European Parliament and active in the Discharge Committee of the European Parliament, began by stating that conflicts of interest exist in all sectors, be it pharma, food, agriculture, tobacco or others. He recalled that, in the case of EMA, their 2011-2012 budget control was suspended due to their unsatisfactory handling of potential conflicts of interest. Improvements have been implemented since then, which goes to show that the Discharge Committee has an extremely important function, namely to assess the hazard of conflicts of interest, in order to evaluate whether society gets value for money when it comes to medicines.

The system's checks and balances

Noel Wathion stressed that contacts between EMA and pharmaceutical companies are essential for EMA's work; without them, EMA cannot do its work properly. However, it is EMA's duty and responsibility to manage potential conflicts of interest properly and to ensure that its work remains independent. To achieve this, EMA has a system of checks and balances, e.g. robust design of scientific advice and assessment procedures, peer review procedures, rules of engagement with the pharmaceutical industry, transparency on stated interests of its experts, and transparency of assessment reports, meeting agendas, and minutes. He

emphasized that thanks to these procedures, no single person can influence decision-making within EMA.

Since 2016, all clinical data that pharmaceutical companies submit to EMA as part of their Market Authorization Application documentation must be [published](#) – an important transparency development. Wathion is proud that EMA is the first regulatory body in the world to do so, and he challenges medicines researchers to reassess this data, in order to verify EMA's conclusions.

Martin Seychell focused on the fact that European institutes interact continuously with all kinds of groups in society: patient organization, NGOs, academics, national health systems, and yes, also pharmaceutical companies. "They all support us as well as challenge us, and so they should. Such discussions are healthy, and will lead to better systems. But it is important to respect each other's roles and responsibilities, and foster trust in the institutions." DG SANTE and EMA continue to improve their transparency, rules and protocols to avoid conflicts of interests and undue influences.

Fergal O'Regan stated that the Ombudsman office has been working with EMA on conflicts of interest and transparency issues for over ten years. The transparency requirements are challenging, but they need to be met, in order to maintain the public's trust in the medicines and vaccines authorized by EMA. He referred to the adaptive pathways mechanism, which states that post-market data on a medicine's effectiveness should be made publicly available and that these data should be used to reconsider market authorization, if need be. This is currently not always the case, which undermines EMA's credibility.

Law as the starting point

Questions from the public addressed the extensive presence of pharmaceutical industry's experts in EMA's expert panels and their dominant influence in clinical trials, and in EMA's protocols and budget. Wathion remarked that EMA, in its way of working and its financing mechanism, follows the law as determined by the European Parliament. If change is needed, then the law needs to change first. He also challenged the audience to name experts who are truly independent; it is a fact of life that most experts are somehow affiliated with the pharmaceutical sector. O'Regan added that the Ombudsman's role is to register declarations of interests, not conflicts of interests. Of course, it is essential that people do not put themselves in situations where these interests become controversial or conflicting. This should be monitored closely.

Yannis Natsis kicked off the second panel by reiterating the need for trust in the European Medicines Agency (EMA). He highlighted the need for a critical review of the top EU regulator, which is why he very much welcomed the discussion, describing it as long overdue. He reiterated that although EMA is primarily a technical and scientific body, its decisions have far-reaching economic and policy consequences. He emphasized the need to break down the silos between national medicines agencies, health technology assessment (HTA) bodies and ministries of health. This should guarantee that the public is able to send the right signals to the market, and ask the right questions in the drug approval process - for the benefit of all patients.

Half of new medicines are ‘nothing new’

Dick Bijl, on behalf of Wemos, referred to publications on the added therapeutic value of new drugs on the market, citing that only 30% were found to be ‘possibly to really helpful’, 51% could be described as ‘nothing new’, and 14% were considered ‘not acceptable’. He underlined the importance of independent clinical trials, as they have been proven to consistently yield clearer results and less false positive outcomes than research that has been financially supported by the pharmaceutical industry. European politicians should therefore facilitate the legal possibilities for EMA to demand from the industry that it includes independent trial data in its market authorization applications. Drug trials should also focus on direct comparison with existing treatments, instead of placebo-controlled design, which obviously yields more positive results.

Accelerated approval for drugs

Silvio Garattini presented additional information in support of Bijl’s statements. He mentioned that accelerated approval has taken place for drugs that had not even reached the Phase III trials stage, meaning that they had not been investigated according to agreed standards of quality, efficacy and safety. Still, they were admitted to the market. He reiterated Bijl’s point of view that the need to consider added therapeutic value of new drugs is of direct interest to patients’ and public health needs.

His concrete recommendation is to create a renewable fund of at least 1 billion Euros (amounting to less than 0,3% of the EU’s pharmaceutical market) for undertaking non-profit independent research. He suggested to learn from the United States, where programs have been set up for direct comparison trials. Garattini also pointed to the increasing dependence of EMA on money from the pharmaceutical industry, these days being over 83% of the overall budget, and to other ways in which the industry is gaining influence over EMA policy, which poses a risk for conflicts of interest.

Higher standards are necessary

Questions from the audience fueled the discussion about some interesting points. **Seychell** remarked that ‘me-too’ drugs - medicines that are very similar to existing drugs, and with little to no added therapeutic value - drive prices down, which is positive in itself. However, **Garattini** believed that by demanding that me-too drugs are better than placebos, the bar is set very, and unacceptably, low. We should demand better than that, as we are basically rewarding pharmaceutical companies for sloppy research by allowing new drugs with hardly any added value on the market. We need to find ways of incentivizing the industry to invest in the development of innovative drugs for real and unmet medical needs.

Value for money

Wathion remarked that for market authorization to be granted, the data on the benefit-risk-ratio need to be robust; this also holds true for me-too drugs. However, he pointed out that it is the responsibility of national health authorities – not EMA’s - to decide whether those drugs are reimbursed in their insurance schemes; in other words, to weigh their medical value against their costs. He again pointed to the possibility of scrutinizing the available clinical data to assess additional criteria of cost-effectiveness.

First steps taken

Wemos was very satisfied with the turnout and interest in the event. Because the European Medicines Agency is moving from London to Amsterdam, we should take the initiative to look for ways in which we can improve EMA policy. Dutch newspapers have reported about [this event](#) and [the lack of added therapeutic value in new medicines](#) on the EU market, and how EMA policy should change. We hope that this event was a first step of the European institutions to improve legislation in order to prevent conflicts of interest in the best interest of patients' health.