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Dear colleagues,

One more time, I have to start our conversation by drawing attention to serious risks that are being imposed on the health and the health law in Brazil today.

Unfortunately we live in a time of distrust on institutions, a scenario where profiteers of all kinds flourish. This is what is happening now with the health legislation in the Brazilian Congress. On April 13, 2016, Brazilian Federal Law n. 13269 was enacted, without vetoes, authorizing patients with cancer to be cared with the synthetic substance phosphoethanolamine. And on April 20, 2016, the Brazilian Federal Senate approved the production and sale of weight-loss drugs containing sibutramine, amfepramone, fenproporex and mazindol. In both cases, the Brazilian National Health Surveillance Agency (Anvisa) – responsible for the registration of medicines, ensuring their quality, safety and efficacy – had spoken unfavorably.

Regarding phosphoethanolamine, in a technical note (56/2015/SUMED/ANVISA), issued in October 2015, Anvisa clarified that there was no granted registration or registration in process for drugs with the active principle of phosphoethanolamine (FOS), and that there was not any clinical research project involving human beings and FOS in the agency. As for the medicinal products containing the substances amfepramone, fenproporex, mazindol and sibutramine, in September 2014, Anvisa adopted its resolution n. 50, issued on 25 September 2014, approving a technical regulation for marketing, prescribing and dispensing control of such drugs, and prohibiting the prescription and dispensing of medicines containing such substances above the Recommended Daily Allowance (RDA).

Firstly, we will examine the case of phosphoethanolamine.

Twenty years ago, a teacher of the Analytical Chemistry and Polymer Technology Group, at *Universidade de São Paulo* (USP), synthesized the phosphoethanolamine. Some people used the capsules containing the substance as if it were a cancer drug. On June 10, 2014, the director of the Institute of Chemistry of São Carlos/USP determined that any activity linked to the production or distribution of drugs and to the drug's therapeutic or sanitary purpose could only happen within that institute after submission to the Board for proper records and licenses. This measure seems to have been the trigger to people having appealed justice for access to pills. Several injunctions were granted, until the President of the São Paulo Court of Justice suspended the effects of the decision, based on the lack of registration of the drug for human use by Anvisa. However, in October 2015, Edson Fachin, Minister of the Brazilian Supreme Court, granted an injunction suspending the decision of the São Paulo Court of Justice

that prohibited the patients to have access to the substance. Also in October, at the Brazilian House of Representatives, it was presented a bill intending to regulate the production and distribution of phosphoethanolamine to cancer patients. On March 8, 2016, the House of Representatives approved a final version of the bill; on March 20 the Senate approved it and on April 13 it was sanctioned and transformed into the Federal Law n. 13269 – which expressly allows the production, manufacture, import, distribution, prescription, dispensing, possession or use of this substance, regardless of legal health register, if clinical studies on this substance were in course (Article 4).

Along with the legislative front, the Executive Power, on 30 October 2015, through the Brazilian Ministry of Health and the Ministry of Science and Technology established a working group to support the necessary steps for the clinical development of synthetic phosphoethanolamine (Ministry of Health Ordinance n. 1767/2015). And on November 16, the Executive Power announced the release of $ 10 million *reais* to finance the initial stages, including the synthesis and characterization of FOS, the non-clinical studies, and the first phase of clinical trials (Phase I). In December, after examining the filed material containing compiled results of studies conducted with the FOS by the group of São Carlos/USP, Anvisa concluded that "the information presented on the phosphoethanolamine is insufficient for assessing the risk/benefit required to start the clinical development" and that the non-clinical development "should be completed with pharmacodynamic, toxicological and pharmacological studies to support the initiation of clinical development". Anvisa also pointed out that decisions on clinical trials and on product registration shall only be taken by the agency and only after full evaluation of the documents submitted by a company able to act in the processes.

In the judicial front, after the publication of the Federal Law n. 13269, in April 2016, the Brazilian Medical Association questioned its legal and constitutional validity through a collective injunction, alleging that the law jeopardizes life, dignity, health and safety, due to the fact that there are no clinical trials related to synthetic phosphoethanolamine and that Anvisa did not evaluate their results to, eventually, grant registration to the drug, in accordance with Article 16 of the Brazilian Federal Law n. 6360/1976. This injunction was not granted for formal reasons ("abstract norms –understood as qualified state provisions connected to the triple attribute of generality, impersonality and abstraction– are not submitted to judicial control using a collective injunction"). However, the same Brazilian Medical Association also sought to challenge the Federal Law n. 13269 in a direct action of unconstitutionality, whose rapporteur, on the Supreme Court of Justice, is the judge Marco Aurélio.

In short, the Brazilian state should not encourage the use of a substance that has not been tested in humans, and that is distributed with no label and no optimal dose indication. But above all, the Federal Law n. 13269 represents a clear disrespect for the role of Anvisa, an institutional agency legally responsible for the technical evaluation of the quality, safety and efficacy of any drug, its registration and marketing authorization.

The same situation happened with the anorexic substances.

Alerted by studies indicating that sibutramine may increase the chance of heart problems in patients with risk factors, Anvisa has forbidden to manufacture, import, export, distribute, handle, prescribe, dispense, sell and use drugs or drug formulations containing the substances amfepramone, fenproporex and mazindol. Moreover, after conducting a technical panel, and a public hearing open to all interested parties, the agency has authorized the prescription, dispensing and delivery of drugs or drug formulations that contained sibutramine only to those that attend to the Recommended Daily Allowance (articles 1 and 2 of the Anvisa's Resolution n. 52, of October 6, 2011). In September 2011 a bill in the House of Representatives prohibiting Anvisa to "cancel the sanitary registration or take any other action to prevent the production or marketing of the anorexic substances sibutramine, amfepramone, fenproporex and mazindol" (PL n. 2431/2011) was presented. The bill was sent to the Senate on July 2, 2015, and was approved with the following wording: "It is authorized the production, marketing and consumption, under medical prescription in the B2 model, of the anorexic substances sibutramine, amfepramone, fenproporex and mazindol". The same bill, with a new redaction, is being examined by the House of Representatives. Note that the text in the Senate fits the technical regulation adopted by ANVISA in September 2014, which only prohibits the prescription and dispensing of medicines containing such substances above the DDR.

It means that there is still a risk of Anvisa's action to be, once again, unauthorized, even with the agency showing great care and respect for the Brazilians, and listening to various stakeholders before adopting the best safety protection of patients using such drugs.

These facts should alert everyone, especially those working in the field of health law, to the need of an effective participation in the discussion of health control measures proposed by Anvisa and, thus, to the defense, by all legally appropriate means, of actions to evaluate the quality, safety and efficacy of any drug, before registering and authorizing its marketing.

Dear readers, I will insist on another point: help us make our *Journal of Health Law* even better! I strengthen the request to send us your articles, reviews or comments to our forensic works section; and your suggestions for topics to be discussed and for names of potential debaters to be included. Do not forget to contribute! The quality of the *Journal of Health Law* also depends on the participation of its readers.

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