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The Mexican General Health Law was reformed on 11th June 2009 to include Article 222*bis*, which defined biotechnological drugs and allowed for the approval of so-called "biocomparables". The decree came into force on 8th September 2009 and the Ministry of Health had a 180-day period to issue all the specific regulations pertaining to the approval of such biocomparables.

The law defines a "biotechnological drug" as any substance produced by molecular biotechnology which has a therapeutic, preventive or rehabilitative effect, which is in pharmaceutical form, and which is identified as such by its pharmacologic activity and physical, chemical and biologic properties.

It also indicates that innovator biotechnological drugs can be used as reference to obtain registrations for non-innovator drugs, which are precisely biocomparables. Other than stating that applications for biocomparable drugs must include the corresponding clinical and *in vitro* studies, the law leaves all specific details to be established through regulations.

Despite the fact that the 180-day period to issue these regulations expired on 8th March 2010, the draft regulations are still being reviewed, with input from both the Mexican Association of Pharmaceutical Research and the National Association of Drug Manufacturers.

COFEPRIS (the Mexican regulatory authority) has made the draft regulations available to the public on the official website of the Federal Commission for Regulatory Improvement (COFEMER)

At present, several interested parties, including pharmaceutical companies, academics and government offices such as the Federal Antitrust Commission, have provided comments on the draft through COFEMER's website. However, as yet there is no certainty as to when the regulations will be issued.

The draft contains the following items:

- A definition of comparability tests between an innovator and a biocomparable drug.

- An indication that biocomparable drugs will use the same name for the active ingredient as the innovator.

- A proposal to eliminate the existing three-year *Roche Bolar*-like research exemption (related to possibility to submit an application for a marketing authorisation before patent expiration, with intent to launch after the date of expiry) so that submissions can now be made at any time. The modification in the corresponding article will also be applicable to chemical drugs.

- A provision indicating that when an innovator or reference drug will be manufactured in Mexico, the pre-clinical and clinical trials must be made locally.

- The timeframes that COFEPRIS will have to approve both innovator and biocomparable drugs.

One of the main hurdles that these regulations have had to overcome are the comments by the COFEMER, which requested, among other issues, the following:

- Justification of the elimination of the three-year period in the *Roche Bolar*-like research exemption in order to verify compliance with provisions in the Industrial Property Law.

- Justification of each requirement to approve biocomparable drugs.

- Additional information on the cost impact that the new regulations will have on industry participants.

- Additional information on reductions of public health expenditure derived from the regulations.

After this information was provided by COFEPRIS, a non-final opinion was issued by COFEMER suggesting changes or clarifications on several issues, including:

- The inclusion of the possibility to take a biologic drug authorised abroad as an innovator/reference drug for the approval of a biocomparable in Mexico, in order to introduce those biocomparable drugs in the market even in the absence of an innovator. This proposal has been analysed by the Mexican authorities in previous years in relation to chemical drugs, without a conclusion being reached.

- The issuance, along with the regulations, of a specific norm to govern pharmacovigilance activities.

- A shortening of the timeframe for approval specified in the regulations, as under the existing system the maximum extension of the relevant deadlines can result in a two-year delay before a biologic drug is finally approved.

- The issuance of regulations which will govern the activities of the New Molecules Committee, which was created in 2008 and has been operating since without specific rules for its operation.

- Since the regulations determine that all interchangeability tests for a biocomparable drug that will be manufactured in Mexico will have to be undertaken within Mexico, COFEMER is recommending a review of this

provision to consider whether all the necessary technology for these tests will be available.

COFEPRIS's response has yet to be made available to the public.

Hitherto, the lack of regulation has generated a degree of uncertainty concerning approvals of both innovator and biocomparable drugs, since analysis of applications has been made on a case-by-case basis. In this regard there has been at least one challenge brought by a research and development company in which the company claimed that the authorisation of a biocomparable was irregular.

It is difficult to estimate when the regulations will be finally issued, since COFEPRIS currently has an important backlog of work derived from renewals of drug marketing authorisation, which were filed in late 2009 and are yet to be resolved. Furthermore, a new head commissioner was appointed recently.

From a legal standpoint, one of the main issues lacking in the draft is a provision contemplating a regulatory exclusivity period as compensation for the expenses incurred in the pre-clinical and clinical trials, which will be mandatory to obtain authorisation for an innovator or reference biotechnologic drug.

The North America Free Trade Agreement, to which Mexico is party, contains provisions contemplating a five-year minimum period after a drug containing a "new chemical entity" has been approved in which no other drug can be approved relying on the information contained in the innovator's dossier.

Whereas this treaty, which came in force in 1994, does not specifically mention biotechnology, the same rationale should come into place on analysis of the regulatory framework that is being established, in which an innovator will necessarily incur high expenses in order to prove a drug's safety and efficacy before COFEPRIS, regardless of whether a patent on the corresponding drug is available.

On the other hand, it is less expensive to prove comparability of a follow-on biologic drug. This unbalance in market entry detracts from the incentive to innovate and bring new drugs and therapies to patients, unless an incentive is

provided to the innovator.

Therefore, the Mexican authorities would be well advised to analyse this issue carefully in order to determine a proper timeframe for regulatory exclusivity after a reference or innovator drug has been approved before a follow-on drug is allowed onto the market based on comparability tests.

Although the previous head commissioner of COFEPRIS indicated that regulatory exclusivity would be provided in a specific provision which is separate from those related to approval, there has been no official statement in this regard by the recently appointed commissioner.

Furthermore, a proposal to change the General Health Law in order to establish a five-year period of regulatory exclusivity for both chemical and biologic drugs is now being studied by Congress.