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For many years, Mexico lacked a particular regulation for biotherapeutic products, specifically those manufactured through biotechnology. Although these products were available for patients in the domestic market, their approval by the Federal Commission for the Protection Against Sanitary Risks (COFEPRIS) was made, until now, under the general statutory framework for chemical drugs. This provided the possibility to obtain marketing authorization for generic versions of these products, relying only on interchangeability tests to prove safety and efficacy.

Recently, this oversight has been addressed by including Article 222 bis in the Mexican Health Law. Although Article 222 is only intended to act as the legal basis for more thorough legislation – which will come with the publication of regulations – Mexico has taken a step towards clarifying the rules applying to these products. This should ensure more accurate treatment from both a scientific and a legal point of view.

This recent amendment follows the elimination of the so-called *requisito de planta* (plant requirement – an obligation to have a manufacturing plant within Mexican territory, either to completely or partly manufacture a drug). It allows drugs companies from all around the world to import and market both chemical and biotherapeutic medicinal products, subject to obtaining the corresponding marketing authorization in Mexico.

ARTICLE 222 BIS OF THE MEXICAN HEALTH LAW

Following international trends, and after a lengthy process in which several industry participants were heard, the Mexican Congress determined earlier this year to address the issue, introducing a new article in the Law that contains a specific definition for these products and providing guidelines on aspects concerning their development, authorization and introduction into the market. Congress has also ordered the Ministry of Health to issue specific regulations on the subject. The Article (see box for text) came into force on September 8, 2009.

There are several issues that become relevant with the coming into force of this article, which will have an impact on the industry and the market.

DEFINITION OF BIOTECHNOLOGICAL DRUGS

The article begins by providing a definition and indicating that drugs produced through molecular biotechnology are to be regulated. Other biologic products could be considered as excluded from this article.

DEFINITION AND ALLOWANCE OF BIOCOMPARABLE DRUGS

The definition of biocomparable drugs is new in itself, as these have been defined alternatively in other jurisdictions as “follow-on”, “biosimilar” or “subsequent entry” products. Regardless of the chosen term, it must be noted that:

1) Reference to innovator drugs is allowed for the authorization of biocomparables.
2) The nature and amount of studies that will be necessary for the approval of biocomparable drugs is not defined. From the article’s wording it would seem that clinical trials are necessary every time, and *in vitro* studies only on certain cases.

LACK OF ESTABLISHMENT/RECOGNITION OF DPE RIGHTS

The issue of data package exclusivity (DPE) has not been defined in Mexico. Whereas confidentiality concerning data submitted to obtain drug marketing authorizations is recognized and protected by the health authorities, there is no specific legal or regulatory framework setting forth a non-reliance period, even though this is a NAFTA-derived obligation.

Even though there have been initiatives to implement DPE through the Health Law or its regulations, none of them have come to pass, and the position of the Ministry of Health is that reliance in an innovator’s dossier is allowed at any time, as long as confidentially is not breached.

Some innovator companies have attempted court actions to obtain recognition of DPE for certain chemical medicinal products, base on provisions in international treaties such as NAFTA and TRIPs, and injunctions have been

ordered forbidding the Ministry of Health to grant authorizations for generics but these actions have not yet been decided.
Therefore, in our opinion, implementations and recognition of DPE rights in biotherapeutic products will not take place in Mexico in the short term.

DRUG SUBSTITUTION

The Article uses the same denomination and the same code as the *Cuadro Basico de Medicamentos* (the basic chart used by public entities to purchase drugs for the public health sector) for innovator and biocomparable drugs. The determination that innovator and biocomparable drugs are equal for the purpose of identification by name and public acquisition code purposes was taken by Congress after hearing arguments from the branded and generics industries.
This would, in principle, permit drug substitution in public acquisitions. The issue of drug substitution by physicians or pharmacists has not been addressed yet, but the pending regulations are expected to contain provisions in this regards.

THE APPROVAL PROCESS

The Article makes reference to the New Molecules Committee, which was created through a regulatory reform in 2008, as the office in charge of determining the approval process for innovator drugs. The jurisdiction of this committee is broadened, as it is now entrusted with analyzing applications for both innovator biotechnological and biocomparables, including determining the amount and nature of the studies that will be required to approve the latter.
For this purpose, a Subcommittee of Evaluation of Biotechnological Products is created. The transitory provisions of the decree through which Article 222 bis was published mentions that this subcommittee must include member of Mexico’s two top public universities.

PENDING REGULATIONS

There has been an impasse over the regulations that will be necessary to

implement Article 222 bis and constitute the regulatory framework for innovator and similar biotherapeutic products. According to the decree through which the Article was published in the Official Gazette, the Ministry of Health was granted until September 8, 2009 to issue the specific Regulations of the New Molecules Committee, in matters applicable to biotechnology drugs, and a period of 180 days to issue the necessary norms and additional regulations, which would complete the statutory framework.

The New Molecules Committee, which was created through a reform to the Health Law Regulations in January 2008, has yet to issue its general regulations, and has been operating on a case-by-case basis, which has been of course a matter of concern as far as legal certainty for industry participants is concerned. These regulations were supposed to be issued by June 2008.

Therefore, the deadlines set forth with the creation of Article 222 bis will most likely not be met, and it is hard to predict when these regulations will be issued, as lobbying efforts by industry participants and consumer groups have been focused on their specific provisions.

The regulations will have to address issues such as clinical and non-clinical evaluations, pharmacovigilance, prescribing information, labels and product substitutions.

IN THE DARK

Aside from the issues that will arise with the regulatory framework for biotherapeutic products as a consequence of Article 222 bis, the main problem at this stage is the lack of specific regulations, leaving industry participants in the dark concerning actual rights and possibilities to obtain authorizations for similar biotherapeutic products.

It will also be important to see if the pending regulations adhere to WHO recommendations, and if any form of DPE is included in them. Pending court proceedings could have an impact in this issue.

The impact of eliminating the *requisito de planta* will also lead to more applications for marketing authorization referring to biotechnology drugs. Therefore the regulatory framework will be paramount to ensure the safety and efficacy of all approved products.