MANUFACTURING OF MEDICINAL PRODUCTS FOR HUMAN USE IN TURKEY

The globalization trend that has gathered momentumduring the last quarter-century has been interrupted by global financial crises and tensionsin the internationaltrade seen over the last years. Domesticmanufacturingisnow givenmore importance in many countries, and studies are conductedwith a view to strengthening domestic manufacturingparticularly of basic necessities such as nutrients and medication. It is expected in the short to medium term that the COVID-19 pandemic, which has influenced the globe starting from the first months of 2020 will increase the localization trend interms of the manufacturing activitiesin the health sector. Correspondingly, it will not come as a surprise that policies are adopted to incentivize the localization of medicine production in Turkey in the upcoming period, as was the case in the recent years.

One of the mainpiece of legislation regulating the medicine production in Turkey is the Regulation on Manufacturing Plants of Medicinal Products for Human Use (the "**Regulation**"). Matters such as the rules to be followed during the manufacturing process, quality management of the manufactured medicinal products for human use, good manufacturing practices, risk management and procedures are regulated -alongside the Regulation- in Good Manufacturing Practices Guideline (the "**Guideline**") which includes parallelprovisions to the related European Union directives.

Manufacturing of medicinal products for human use is acomprehensive process, various aspectsof which are regulated in detail in the Regulation and the Guideline. This articletouches base toobtaining of manufacturing plant authorization, which is a crucial step of the manufacturing process as well ascontract manufacturing conducted by holders of suchauthorization on behalf of license holders, which is commonly seen in practice.

Obtaining manufacturing plant authorization.In order to manufacture medicinal products for human use, real or legal persons who will conduct the manufacturing shall apply to the Turkish Medicine and Medical Devices Institution (the "**Institution**") to obtain a manufacturing plant authorization.Manufacturing plant authorization is exclusively grantedfor the manufacturing plant, the relevant manufacturing activity and the medicinal product for human use to be manufactured, which are specified in the application. In case of a change in the manufacturing plant, manufacturing procedures or in the product to be manufactured upon the application,suchchange shall be notified to the Institution and an application for additional authorization may be required. In order for the manufacturing plant authorization to be issued (i) all the documents indicated in the Regulation must be submitted to the Institution, (ii) it must be concludedby the Institution upon the inspections that the manufacturing plant is qualified to fulfil the requirements set forth in the good manufacturing practices, and (iii) the applicant must employ a responsible manager, production manager, quality assurance manager, quality control manager and sufficient number of suitablepersonnel within its organization. Following the issuance of the authorization, the applicant shall be responsible for manufacturingthe products within the scope of the authorization in accordance with the legislation, the Guideline and the product license, and must keep its manufacturing methods up to date in line with the scientific and technical developments.

Contract manufacturing of medicinal products for human use. As can also be understood from the above, manufacturing of medicinal products for human use can be conducted only by the manufacturing plantauthorization holder and holding the manufacturing authorization is rather essential for manufacturing purposes than holding the license of the product. As a matter of fact, nowadays, many license holders of medicinal products for human use have their products manufactured by third party manufacturing authorization holders under contract manufacturing agreements. Thus, license holders who do not prefer to employ the required personnel andto

maintainsuitablefacilities within their organization or who decide not to conduct the manufacturing themselves as part oftheircommercialplanning, may seek to procure the manufacturing from third parties. For the contract manufacturing of the relevant medicinal products for human use to be conducted within this scope, the rights and obligations of the parties must be explicitly and clearly regulated under a written contract to be executed between the license holder and the manufacturing authorization holder. The contract, which will also need to be submittedto the Institution upon execution, must provide in detail for, among others, complaints, withdrawals, contracted analyses and quality related matters,that the contractorshall observe the good manufacturing practice principlesand of which party's responsible managershall be in charge of the release of each batch.

In case of contract manufacturing of the medicinal products for human use, the responsibility of the manufacturing authorization holder is limited withensuring that the manufacturing plant is in compliance with the legislation and the manufacturing activities are carried out as per the legislation and good manufacturing practices. As the license holder is essentially responsible vis-a-vis the Institution and third parties during the process starting from the manufacturing of the products up to the consumer use,it is imperative for the license holders tocloselymonitor the manufacturing process.

As mentioned above, regardless of holding the license of the medicinal product for human use, a manufacturing plant authorization must be obtainedin order to manufacture the relevant products. To obtain such authorization, it is substantial to ensure,among others, that the plant and the personnelare in compliance with the Regulation and the Good Manufacturing Practices Guideline and that the manufacturing is scientifically and technically up to date. The contract manufacturing method, which is used in many areas today, enables the license holders in pharmaceutical industry to benefit from theproduction activities of the manufacturers, whose plants and personnel are structured in a way that is suitable for the manufacturing of medicinal products.