Current Good Manufacturing Practices and Distribution Agreements

cGMP: Introduction

The main regulatory standard for ensuring pharmaceutical quality is the Current Good Manufacturing Practice (‘cGMP’) regulation for human pharmaceuticals. In the United States of America, the Food and Drug Administration (the ‘FDA’), and in the European Union (‘EU’), the European Medicine Agency (the ‘EMA’), regulate pharmaceuticals that are manufactured or sold in each of these jurisdictions. Consumers expect that each medicine they take is safe and effective, regardless from which batch of medicines or manufacturer it originates.

The importance of regulating the manufacture and distribution of pharmaceutical products cannot be overstated.

However, an array of laws, regulations, directives, and guidelines surrounding cGMP have been issued by regulatory authorities throughout the world, which seek to govern, and develop, the production, storage, distribution, and supply of pharmaceutical products. Often, there is no mutual recognition agreement in place between jurisdictions thus, a manufacturer may be required to meet the cGMP regulations in its country of manufacture, but also in the country into which the products are distributed, as local cGMP compliance is often a pre-condition for obtaining product marketing authorisation (‘MA’) within a jurisdiction.

WHO and Quality Assurance Principles

The World Health Organisation (the ‘WHO’) has a duty to develop, establish and promote international standards in relation to pharmaceutical products (Article 2(u) of the Constitution of the WHO). Consequently, its version of good manufacturing practice guidelines is used by pharmaceutical regulators in over 100 countries however, sometimes it is only applied in part.

The WHO promotes Quality Assurance to the production and control of pharmaceutical products on the

basis of the core principles of Quality Management and Quality Controls. The WHO stipulates that cGMP is part of the Quality Assurance, and as set out in Annex 3, WHO Good Management Practices for Pharmaceutical Products: main principles, such practices include that:

1. ‘manufacturing processes must be clearly defined, systematically reviewed in the light of experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications;
2. qualification and validation are performed;
3. all necessary resources are provided, including:
    1. appropriately qualified and trained personnel;
    2. adequate premises and space;
    3. suitable equipment and services;
    4. appropriate materials, containers and labels;
    5. approved procedures and instructions;
    6. suitable storage and transport; and
    7. adequate personnel, laboratories and equipment for in-process controls;
4. instructions and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided;
5. operators are trained to carry out procedures correctly;
   records are made (manually and/or by recording instruments) during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and quality of the product are as expected; any significant deviations are fully recorded and investigated;
6. records covering manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form;
7. the proper storage and distribution of the products minimises any risk to their quality;
8. a system is available to re-call any batch of product from sale or supply; and
9. complaints about marketed products are examined, the causes of quality defects investigated, and appropriate measures taken in respect of the defective products to prevent recurrence.’

United Arab Emirates (‘UAE’)

In the UAE, a manufacturer may apply for a ‘Certificate of Compliance with cGMP’ with the Drug Control Department of the Ministry of Health and Prevention, for which Gulf Co-operation Council (‘GCC’) and WHO Standards apply.

Any industry player clearly requires an in-depth knowledge of the relevant regulations and standards, including all developments, in order to manufacture and distribute its products within the GCC.

Agency and Distribution Network

Manufacturers will rely upon an agency and distribution network to market, promote and sell its products.

These arrangements, whilst common in practice, can be complex and require careful and regular monitoring and review so as to ensure that the parties do not fall foul of applicable laws and regulations in relation to the marketing and sale of its products.

Products will be transported, stored and sold, in various jurisdictions, by third parties along the supply chain. Therefore, there are numerous opportunities and possibilities for products to become ‘cross-

contaminated' under cGMP and, in such circumstances, manufacturers and/or distributors may find themselves liable to pay damages and/or penalties. In addition, in some cases, criminal liability may arise.

Further, an agent or distributor may be responsible, whether under contract or law, to ensure that the pharmaceutical products being marketed in its territory are registered with the local health authority (or a similar agency), and such registration will be contingent upon the products being manufactured under cGMP applicable in that jurisdiction.

Therefore, these supply network agreements should specifically deal with and provide for, as far as possible, requirements under cGMP, including provision to deal with complaints and re-call of products, storage requirements and standards and the sharing of general information and records of sales.

Each party will also seek to protect itself against the other's acts or omissions by way of indemnification (if possible in the relevant jurisdiction) and insurance.

Conclusion

The manufacture, marketing and sale of pharmaceutical products is, understandably, highly regulated and safe distribution requires careful consideration and implementation of Good Manufacturing Practice.

cGMP requires implementation along the entire supply chain and, therefore, it is important that manufacturers, agents, and distributors of these products provide for compliance, in so far as possible, within contractual arrangements.

Al Tamimi & Company's Healthcare Practice in Ras Al Khaimah regularly advises on laws and regulations impacting the healthcare sector. For further information please contact healthcare@tamimi.com.