**GOOD MANUFACTURING PRACTICE (GMP)**

All stages of antibiotic production from fermentation through to finished product are governed by the code of GMP, of which quality control is an aspect. GMP requires that there should be a comprehensive system, so designed, documented, implemented and controlled, and so furnished with personnel, equipment and other resources as to provide assurance that products will consistently be of a quality appropriate to their intended use.

Quality control is concerned with testing the quality of the product by a combination of in-process and final product testing. However, that a product meets specification does not necessarily mean that it is suitable for use. GMP is about ensuring that quality is built in to all stages of the manufacturing process. The following are basic GMP requirements outlined in the Medicines Control Agency Rules and Guidance:

1. All manufacturing processes should be clearly defined and be capable of consistently producing material of the required quality and complying with specifications.
2. Critical steps of manufacturing processes and significant changes to processes should be validated.
3. All necessary facilities for GMP should be provided including:
4. Appropriately qualified and trained personnel
5. Adequate premises and space
6. Suitable equipment and services
7. Correct materials, containers and labels
8. Approved procedures and instructions
9. Suitable storage and transport
10. Instructions and procedures are written in an instructional form in clear and unambiguous language, specifically to the facilities provided.
11. Operators are trained to carry out procedures correctly.
12. Records are to be made during manufacture which demonstrates that all steps required by the defined procedures have been taken and that the quantity and quality of the product was as expected. Any significant deviations are to be fully recorded and investigated.
13. Records of manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form.
14. The distribution (wholesaling) of the products minimizes any risk to quality.
15. A system is available to recall any batch of product, from sale and supply.
16. All complaints are examined, the cause of quality defects investigated and appropriate measures taken in respect of the defective products and to prevent recurrence.

Failure to comply with GMP guidelines may result in a manner of sanctions from regulatory authorities, up to and including recall of product from market and withdrawal of manufacturing and marketing licenses. Thus appropriate standards for the manufacture of antibiotics are monitored and maintained.

**BIOTECHNOLOGY IN PHARMACEUTICAL SCIENCES**

Genetic engineering involves altering DNA molecule outside an organism, making the resultant DNA molecule function in living cells. Many of these cells have been genetically engineered to produce substances that are medically useful to humans. Pharmaceutical biotechnology involves the use of living organisms such as microbes to create new pharmaceutical products, or safer and more effective versions of conventionally produced pharmaceuticals, more cost-effectively. Since the manufacture of the first recombinant pharmaceutical, insulin, there has been a burst in the generation of new recombinant drugs and vaccines. One of the pharmaceutical biotechnology’s great potentials lies in gene therapy, which consists of the insertion of genetic material into cells to prevent, control or cure diseases. It encompasses repairing or replacing defective genes and making tumors more susceptible to other kinds of treatment.

Recombinant human insulin was the first drug produced using genetic engineering in 1982, for the treatment of diabetes. Before its production, animals (pigs and cattle) were the only non-human sources of insulin. Theirs differ slightly from humans’, which can elicit immune response against it, when injected into humans, making this insulin ineffective. The use of recombinant insulin prevents all these problems and more.

Another recombinant product is the ‘antigrowth hormone’, somatostatin. This modulates the action of the growth hormone and is frequently used to treat acromegaly (uncontrolled bone growth). Being a very small peptide, the gene coding for it can easily be chemically synthesized and cloned into a suitable expression vector.

Somatotropin, the human growth hormone (hGH) contains 191 amino acids and is produced in the pituitary gland for the regulation of growth and development. Regular injections of hGH are given to children with dwarfism caused by the absence of this hormone, so that they can reach near-normal heights. In this case, animal-derived hormones are ineffective and only the human protein works. Because of the lack of pituitaries from human cadavers, the use of recombinant hGH has been imperative.

**PRODUCTION OF RECOMBINANT ANTIBIOTICS**

A large number of the antibiotics currently used have been isolated from the Gram-positive soil bacterium *Streptomyces*, although other bacteria and fungi have also been used as sources. The biosynthesis of an antibiotic can sometimes include 10 – 30 separate enzyme-catalyzed steps, which makes the cloning of all the genes coding for the enzymes very difficult. A strategy used to isolate the complete set of antibiotic biosynthetic genes consists of the transformation of a recombinant gene library from an organism producing the antibiotic, into a mutant strain of the same organism unable to make this antibiotic. The transformants are screened by plating them unto agar plates already seeded with bacterium sensitive to the antibiotic. The appearance of halos of growth inhibition around the recombinant colonies indicates the successful cloning of the antibiotic biosynthetic gene cluster.

In some instances, rDNA (recombinant DNA) technology has been successfully used to generate novel antibiotics by introducing in the same organism the genes responsible for the synthesis of two very closely related antibiotics. By cross-feeding antibiotic intermediates between two close pathways, novel antibiotics can be generated. This strategy has been very successful using different *Streptomyces* species.

**NEW DIAGNOSTICS USING rDNA TECHNOLOGY**

For many years, clinical diagnostic laboratories had limitations in the detection of pathogenic bacteria and parasites due to time constraints, as they required being cultured. These time-consuming procedures are detrimental to patients’ health. The rapid developments in molecular biology employing techniques such as DNA hybridization and PCR amplification are very helpful in the diagnosis of infectious diseases. There are currently primers and probes for the detection of more than 100 infectious diseases e.g. malaria, Chagas disease, respiratory failure, food poisoning, gastritis, gastroenteritis etc.