3. Design all the steps involved in making the product, e.g. selection following steps:

What do you want to produce in making the product.

4. Specify how the quality of the product’s characteristics and the manufacturing processes are measured and what action must be taken if standards are not met. Ideally, these actions should be built into the whole production process so that they are carried out automatically.

These features may be summarised in the following simplified diagram.

### The role of analysis in Quality Control

You may have carried out simple tests to show the presence of starch, sugar, vitamin C, etc. in various foods. Qualitative tests indicating that various fruits and vegetables contain vitamin C, do not tell you how much vitamin they contain or which foods have the most or the highest concentration; for that, quantitative tests are required.

Modern pharmaceutical analysis involves a range of qualitative and quantitative methods. Qualitative methods determine precisely what substances are present in a product. Quantitative methods assess the concentration of the active ingredient.

#### Qualitative analysis

In school you may have carried out a test for acid using limus paper or a test for carbon dioxide by bubbling it through limewater. Blue limus paper changes to red in an acid. Carbon dioxide makes limewater go cloudy. These are qualitative tests; they indicate the presence of some substance but do not tell you how much is present. Other relatively simple qualitative tests include flame tests and precipitation tests for various anions and cations.

#### Quantitative analysis

- Test the products for purity and impurity (the amount of the active and inactive ingredients and that they are labelled accordingly. Inactive ingredients – called excipients – are commonly added to tablets to give them bulk and to bind and stabilise them. They also facilitate detection of counterfeit products. All the ingredients, both active and inactive, must be of very high purity and be free of harmful contaminants and allergens.

### Product potency – an example

The active ingredient in Tylenol tablets is paracetamol (also known as acetaminophen). Tylenol tablets are produced in a range of strengths, i.e. containing different amounts of paracetamol, working at different age groups: 80 mg, 160 mg, 325 mg, 500 mg. It is clearly important that the tablets or capsules contain the correct amounts of active and inactive ingredients and that they are labelled accordingly. Inactive ingredients – called excipients – are commonly added to tablets to give them bulk and to bind and stabilise them. They also facilitate detection of counterfeit products. All the ingredients, both active and inactive, must be of very high purity and be free of harmful contaminants and allergens.

### Product quality

#### Process Performance

Specify how quality will be measured at each stage of the manufacturing process.

#### Process Design

Design the steps involved in making the product.

#### Product Specification

Define the criteria that the product must meet for each of its desired characteristics.

#### Qualitative tests provide a ‘yes’ or ‘no’ answer to a question such as: ‘Is this solution acidic or basic?’ or ‘Is the product free of E. coli?’.

Qualitative tests are usually easier to carry out than quantitative tests. Qualitative analysis involves a range of tests that are carried out on individual samples, e.g. selecting a sample, testing, packaging, labeling.

#### Quantitative tests involve some measurement of quantities such as mass, volume, concentration, etc. Acid-base or redox titrations that are carried out in school chemistry classes are examples of quantitative analysis.

Their purpose is to measure the concentration of particular solutions.

The classical quantitative methods of analysis include titration, precipitation, filtering and weighing. These methods are still important and are included in school and college courses. Modern analysis includes many instrumental methods such as mass spectrometry, chromatography, electrophoresis and several kinds of spectroscopy.

In contrast to the classical methods, instrumental methods typically require expensive equipment as well as expertise in its use. Instrumental methods can often be used for both qualitative and quantitative chemical analysis.

### Sampling and statistical analysis

Throughout the whole process of pharmaceutical manufacture samples are taken out for inspection and analysis. All samples from a single batch will work exactly the same result; hence there will always be slight variation in the quantities and in the measurements. Statistical analysis is applied to see if the variations are within the expected range.

Since the mathematical formulae used in statistical analysis are valid only for random data, it is vital that the samples are taken randomly.

### MSD Ireland:

MSD Ireland is one of the country’s leading healthcare companies, having first established here over 50 years ago.

We currently employ approximately 2,500 employees, across five sites in Ballydine, Co. Tipperary, Brinny, Co. Cork, Carlow and Dublin and, in addition, operate substantial Human Health and Animal Health businesses. Our new biotechnology facility MSD Biotech, Dublin, is currently under construction and will be completed in 2021, and we are also constructing a second manufacturing facility at our existing site in Carlow with the creation of 170 new jobs.

In total to date, we have invested approximately €3 billion in our Irish operations and our annual turnover ranks us as one of Ireland’s top 20 companies. Our Irish sites manufacture approximately half of MSD’s top twenty products, saving and enhancing lives in over sixty countries around the world.

At MSD, we have and always will be... Inventing for Life. These three powerful words reflect our commitment to inventing new medicines and vaccines that save lives by preventing and fighting disease. MSD has dedicated researchers trained in many different scientific disciplines who work tirelessly to find cures for significant diseases that still afflict millions around the world and we will continue on this path. We offer employees hugely ambitious and exciting career paths for different areas of technology, creating new treatments and products that save and enhance lives, playing a significant role in addressing the world’s most vital, urgent needs.

At MSD Ireland we firmly believe that the most important thing we make is a difference – to patients, to our employees, to our communities and to the Irish healthcare landscape generally.

MSD Ireland is 100% committed to putting the patient at the heart of everything we do and we are also firmly focussed on giving back to the communities that we operate in and bringing real value to the Irish healthcare landscape generally. Over the last five years we have consistently been ranked as one of the top five business contributors in Ireland and over that period our employees have volunteered over 1400 hours to a host of projects. In fact, our employees have helped and supported over 500 local projects and have contributed over €6.5 million to a range of worthy causes and projects.

To learn more about MSD, our operations in Ireland and the career opportunities available, please visit www.msd.ie
The Importance of Quality Control in the Pharmaceutical Industry

Leaving Certificate Chemistry

Instrumental methods of separation or analysis:

1. Mass spectrometry.
2. Gas chromatography.
4. Additional industrial chemistry: Characteristics of effective and successful industrial chemical processes... co-products (separation, disposal or sale)...
5. Infra-red absorption spectrometry.
6. Ultraviolet absorption spectrometry.
7. Chemical or hormonal system, nerve and sense organ.

Additional industrial chemistry: Characteristics of effective and successful industrial chemical processes... co-products (separation, disposal or sale)...

Leaving Certificate Technology

A Process of Design (p. 11 - 13)


Leaving Certificate Biology

Chemical or hormonal system, nerve and sense organ system, muscular, skeletal and an immune system.

Science and Technology in Action is also widely used by Transition Year classes.

Student Activities

1. Quality Assurance focusses on the quality of the manufacturing process while Quality Control focusses on quality of the product. Discuss the importance of these areas for the future of Irish biopharmaceutical industry.

2. How can the contribution of the biopharma sector, both nationally and globally, be developed into the future.

(See pages 3 & 5 of the report of the BioPharma Ambition Conference 2020 here: https://www.biopharmaambition.com/)

3. Find the mass of 10 similar coins, one by one using an electronic balance. Assuming that the accuracy of the last digit is +/- 1, calculate the possible percentage range of the possible error in each case. Then weigh all ten coins together and calculate the possible percentage range of error. Discuss your results.

4. Prepare a set of slides for your class summarising what the work of a Quality Control analyst entails. Online videos such as the following should help: https://www.getreskilled.com/what-is-a-quality-control-associate/

5. The following online video introduces the Deming Cycle: https://www.youtube.com/watch?v=e4gOPeHSRo8

Examination Questions

Leaving Certificate Chemistry 2018 (HL) Q. 4 f

By referring to the diagram of the infrared spectrum of aspirin, or otherwise, give a simple explanation of the principle of infrared spectrometry.

Leaving Certificate Chemistry 2009 (HL) Q. 7

According to the EPA (Environmental Protection Agency) publication 'The Provision and Quality of Drinking Water in Ireland (2006-2007)': Drinking water must be clean and wholesome. That means it must meet the relevant water quality standards and must not contain any other substance or microorganism in concentration or numbers that constitute a potential danger to human health.

(i) Describe how suspended solids are removed in water treatment.
(ii) What treatment is carried out to ensure low levels of micro-organisms in drinking water?
(iii) What problems would arise if the pH of a public water supply were outside the range 6 – 8?
(iv) EU standards specify that the concentration of lead (in the form of Pb²⁺) in drinking water must be below 10 µg/l. Why must the Pb²⁺ concentration be kept so low? How are levels of Pb²⁺ removed from large quantities of water?

Leaving Certificate Technology 2017 (HL, B) Q. 4 b iii

(iii) A Quality Control scheme is in operation for a process which produces ball bearings. Each hour 6 bearings are taken and their diameters measured. The process delivers a mean diameter of 20 mm with a standard deviation of 0.03 mm. The lower and upper specification limits are 19.97 mm and 20.01 mm respectively.

Calculate the process capability index and give the 'control range' of the process, where: Cpk = \( \frac{\text{mean} - \text{lower limit}}{3 \times \text{std dev}} \).

Leaving Certificate Technology 2014 (HL, B) Q. 8 b ii

Explain the purpose of a Quality Control (QC) system in product manufacture.

Leaving Certificate Technology 2019 (OL, B&C) Q. 6

Manufacturers of commercial sensor alarms use quality management techniques to ensure that their products are of the highest quality. The Deming Cycle focuses on continuous improvement and consists of four stages: Plan, Do, Study and Act.

(i) Briefly outline any two of the stages of the Deming Cycle.
(ii) Outline two consequences for a company that manufactures faulty goods.

Did You Know?

Biopharmaceutical manufacturing in Ireland

- "Ireland has a large biopharmaceutical manufacturing presence relative to other sectors and to other similar-sized countries.
- "The industry is responsible for over 45,000 jobs and accounts for 62% of the country’s exports. Its presence is regionally distributed.
- "This cannot be taken for granted. The biopharmaceutical industry is not static and now is not a time for complacency...
- "As sectors like technology, medical technology and biopharmaceuticals converge, similarly the gap between industry, policy, research and clinical leaders is narrowing. ...
- "We must focus on driving innovation, connecting and aligning key players across sectors, and work on enhancing Ireland’s reputation for life sciences and competitiveness proposition.”


Biographical Notes

Diarmuid Buckley – QC Microbiology Analyst, MSD Brinny

Diarmuid joined MSD in July 2018, having previously worked as a Student Intern in the same role at MSD for 6 months in 2017. He then completed his final year college project in MSD at the start of 2018, titled ‘The long-term storage of Bacterial Isolates, and the effects of this on their viability.’

Diarmuid graduated from Cork Institute of Technology in May 2018 with a bachelor’s degree in Pharmaceutical Biotechnology. This course allowed him to develop broad expertise across Microbiology, Chemistry, and Biochemistry. These skills are invaluable for the pharmaceutical sector.

He works with a diverse team based in the QC Microbiology laboratory at MSD Brinny, Co Cork. His role includes the sampling and testing of water systems across the site to ensure their quality – a crucial part of the manufacturing process.

Revise The Terms

Check the meaning of the following key terms:

- anions, assay, cations, chromatography, counterfeit, criteria, double blind trials, electrophoresis, ELISA, excipients, flagship product, litewater, mass spectrometry, medical practitioner, mg, paracetamol, pharmaceutical, precipitation, qualitative, quantitative, redox, spectrosopy, titration.

Check the Glossary of terms for this lesson on www.sta.ie

True/False Questions

a) A high quality pharmaceutical product is one that is both safe and effective.

b) High quality products benefit the consumer but not the producer.

c) Quality is subjective and so cannot be measured.

d) Quality by Design eliminates the need for testing.

e) Quantitative tests involve some measurement of quantities such as mass, volume, concentration, etc.

f) Mass spectrometry, chromatography and electrophoresis are instrumental methods of analysis.

g) In a ‘double-blind trial’ the patients don’t know if they have received the real product or not, but their doctors do.

h) The potency of a pharmaceutical product is the minimum amount of it that is effective, for 50% of recipients.

i) School chemistry practicals involve both qualitative and quantitative analysis.

j) Litmus paper gives quantitative results.

Check your answers to these questions on www.sta.ie.