

GENERAL QUESTIONS ON PLANT MOLECULAR FARMING (PMF)

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GENERAL QUESTIONS AND ANSWERS ON PLANT MOLECULAR FARMING (PMF)

1. What is Plant Molecular Farming (PMF)?

Plant Molecular Farming (PMF) is the production of drugs using genetically engineered plants.

Other terms used for PMF are "molecular farming", "molecular pharming", "plant molecular pharming", or "biopharming".

Genetic modification is any intentional change to genetic material, and it comes in many forms. Farmers have used **conventional breeding methods (artificial selection)** for thousands of years to change genetic material by transferring desirable traits from one plant to another. Conventional breeding techniques involve the mixing of thousands of genes. **Artificial mutagenesis** occurs when cells are treated with external agents, like ultraviolet light or certain chemicals, to produce a change in genetic material. **Genetic engineering** is the introduction of a gene or genes into a plant to produce a change in genetic material. Genetic engineering is more precise than conventional breeding techniques as it targets specific gene(s). Genetic engineering technology has been used for decades, and it is the application in plants to produce drugs that is a more recent development.

2. Why would drugs be grown in plants?

There are expected to be several potential advantages to growing drugs in plants including faster drug production, higher volume of drug production, and cheaper drug production.

3. How are drugs grown in plants?

Plants are used as the manufacturing machinery to produce proteins used in drugs. These drug proteins are expressed in plants cells, plant tissues, or whole plants, which may be grown on a large scale. The protein is extracted and purified from the plant to make the drug.

The same concept of manufacturing applies to most biologic drug production platforms. Many drugs, such as hormones, enzymes, antibodies, and vaccines, are products of genetic engineering in microorganisms or animal cells. Since the 1980's, diabetics have used insulin produced from bacteria and yeast that have been genetically engineered with a human insulin gene. The biochemical machinery of the host cell translates the inserted gene into the corresponding protein. The genetically modified organisms are produced at large scale in bioreactors, and then the desired protein is isolated and purified.

The difference between PMF and other drug production platforms is the "machinery" or "factory" - the protein expression happens in a plant instead of in bacteria, yeast, or animal cells.

4. What are plant-derived biologic drugs?

A biologic drug (Schedule D drug as defined by the *Food and Drugs Act*) is made from or through the use of living organisms e.g., bacterial or animal cell cultures, in contrast to a chemically synthesized drug. A plant-derived biologic drug is a biologic drug that is made using PMF.

Examples of drugs that could be made from a plant platform are vaccines, insulin, monoclonal antibodies, and hormones.

Other terms used for plant-derived biologic drugs are "plant-made pharmaceuticals", or "biopharmaceuticals".

5. Are plant-derived biologic drugs as safe as other biologic drugs?

Biologic drugs produced from plants are comparable to drugs produced from other biologic drug production platforms, like bacterial and animal cell cultures. Plant-derived biologic drugs are subject to the same regulations and the same process for obtaining market authorization in Canada as other biologic drugs. Health Canada applies the same rules and standards of safety, efficacy, and quality.

6. How are plants that are used to produce plant-derived biologic drugs and the plant-derived biologic drugs themselves regulated in Canada?

Several Government of Canada Departments and Agencies are responsible for plant-derived biologic drugs in Canada with respect to the product (i.e., safe drug) and the environment (i.e., no contamination in the environment, in the food chain, nor from disposal of plants that were used to produce plant-derived biologic drugs).

Health Canada is responsible for the approval of plant-derived biologic drugs, and ensures the safety, quality, and efficacy of these products in Canada.

Environment Canada and Health Canada jointly oversee the environmental and indirect human health assessment of new substances (e.g., human exposure via drinking water, soil or air). The Pest Management Regulatory Agency (PMRA) oversees pesticides applied to the plant from which the drug was derived. The Canadian Food Inspection Agency (CFIA) oversees environmental release, like research field trials or crop residues; and that products, by-products, or waste materials of PMF production cannot be used as livestock feed or other secondary commodities (e.g., fertilizers, composts). Environment Canada, Health Canada, and CFIA oversee the disposal of plants used to make plant-derived biologic drugs.

Plant-derived biologic drugs are being produced inside contained facilities, like bioreactors and greenhouses. In the future, PMF plants may be grown commercially outside in confined fields with specific restrictions.

7. Why does Health Canada have a specific Guidance document about PMF?

PMF is a novel platform that has some manufacturing differences in comparison to conventional drug production platforms. The key manufacturing differences lie in the plant growth and harvest stages, and in how to establish product purity and quality. The Guidance therefore helps manufacturers interpret current requirements under the *Food and Drugs Act* and Regulations in order to apply them to plant-derived biologic drugs.

8. Will the PMF origin of plant-derived biologic drugs be identified?

Manufacturers are not required to indicate the specific production platform on the drug container label (e.g., bacterial cell culture origin, yeast cell culture origin, animal cell culture origin, or plant origin). Information on how a drug is produced is usually presented in each drug's Product Monograph, which is available to the general public. Any potential allergen risks are considered in drug evaluation and labelling.

Regardless of origin (e.g., bacterial cell culture origin, yeast cell culture origin, animal cell culture origin, or plant origin), all drugs must meet the same safety, efficacy, and quality standards in Canada.

Like with other biologic drugs, plant-derived biologic drugs can be traced by their drug identification number (DIN) on the drug's label and by lot number.

9. Why are plant-derived biologic drugs not natural health products (NHP)?

Natural health products are naturally occurring substances. The proteins expressed in genetically engineered plants and used to make plant-derived biologic drugs are not naturally expressed in those plants.

10. Are there plant-derived biologic drugs available in Canada?

Several plant-derived biologic drugs are in development. Plant-derived biologic drugs have been used in clinical trials in Canada since 2010.