wjpmr, 2021,7(13), 5 – 7.

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

GMP VS GACP; GACP AND THEN GMP OR HARMONIZING GACP AND GMP?

Dr. François-Xavier Lacasse*

Faculty of Pharmacy, University of Montreal, Montreal, Hemione Inc., Pharmafrican Inc., Canada.

***Corresponding Author: Dr. François-Xavier Lacasse**
Faculty of Pharmacy, University of Montreal, Montreal, Hemione Inc., Pharmafrican Inc., Canada.

Article Received on 28/09/2021 **Article Revised on 18/10/2021** **Article Accepted on 08/11/2021**

INTRODUCTION

During the last decades, marketed drugs were mainly composed on small molecules and biologics. Then, biological molecules became more and more popular, followed by biosimilars. A lot of people thought that small molecules were declining…. but it was not the case for goods reasons: tablets and solid oral dosage have been and will remain successful, because of its ease of administration, the patient's compliance, and the overall efficacy. It must be admitted that progresses have been made in orally dosed macromolecules such as oral insulin,[1] and oral COVID-19 vaccine,[2] just by checking the numerous clinical trials that have been carried out recently. In parallel to these chemical and biological drug developments, botanical plants have generated an increasing interest. According to FDA guidance entitled Botanical Drug Development Guidance for Industry,[3] "*the term botanicals means products that include plant materials, algae, macroscopic fungi, and combinations thereof*". This guidance describes all the steps (chemical, non-clinical and clinical) that are needed to streamline the development of a plant into a drug product. When the word "drug" appears somewhere, it will be automatically and indefectibly associated with the Good Manufacturing Practices,[4] or GMPs, and more recently the Quality by Design,[5] or QbD, that shows how to develop a drug product with a full understanding of the critical quality attributes of the compounds that cannot be dissociated duringthe development with the main critical manufacturing parameters. With botanical drugs, another step was born that will give a full traceability of the plant, starting from its seeds, the way they been collected, harvested, and planted, to its growing and final collection. These steps are now managed by the Good Agriculture and Collection Practices (or GACP).[6]

That being said, if the need is to get a botanical product on the market, is there a need to follow GACP and GMP, or only GACP, or only GMP, or GACP and then GMP or to harmonize GACP and GMP? It may be easier to answer this question if you know the clients' needs, whether they are planning to file functional food, nutraceutical, cosmeceutical, or biopharmaceutical products:

- For a raw material substance, i.e., leaves or crude plant, GACP should drive the whole harvesting since the client will then be responsible of treating the bulk.
- For a semi-finished product, for instance plant extracts, once again, harvesting will follow the GACP and then the GMP should be followed. It must be noted that Health Canada launched in 2004 a guidance on natural health products (NHP) on which cGMP for NHP are described. Even though this guidance is not restrictive as the cGMP for drugs is, the "cGMP way of thinking" is definitely part of this document. Furthermore, regarding plant extracts, the most important questions are the following:

- Any literature on the plant and its extracts?
- How many extracts in the plant?
- How many of interest to be extracted?
- What about the physical state of the extracts? Oil? Powder? Liquid crystal? Impact of the extraction on the solid-state chemistry of the powder extracts: Is polymorphism important?
- Solvent(s) for extraction: Is there a need to use something else than class 3 solvent, as per ICH guidelines ?[7]
- What will be the rate of extraction for each extract? The amount of raw material may vary drastically from one plant to another.
- Is there a synergy between extracts? i.e., some extracts are working with eachother and may not be as effective if they are isolated from each other.
- Recycling (extraction's wastes) cycle is possible?

By looking at the above listing, careful attention should be paid and therefore the cGMP and the QbD should be highly followed to obtain robustness, reliability, and reproducibility whereas the GACP will ensure the full traceability.

The Table 1. Below,[8] illustrate not only the differences between GACP and cGMP but also where the gap

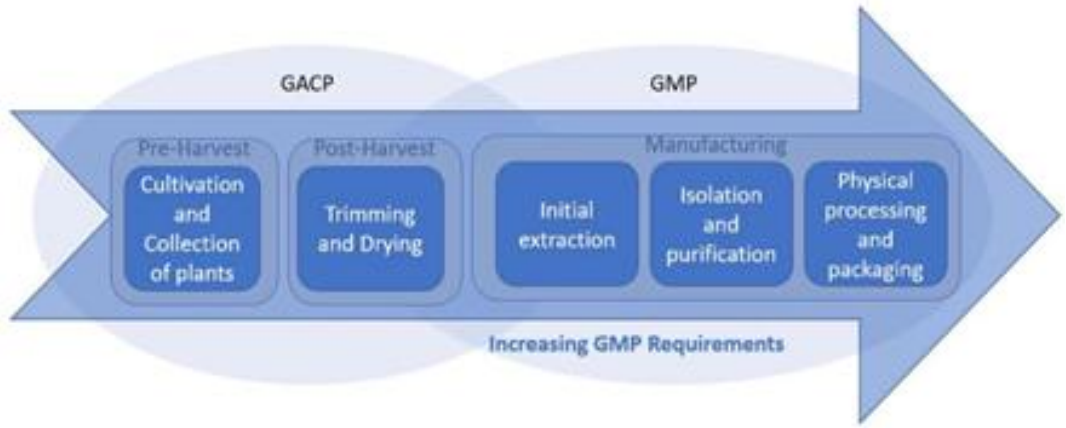
between, surrounded in blue, where both must be bridged to streamline any product development process.

Table 1: Difference between GACP and GMP and their commune area.

Activity	Good Agricultural and Collection Practice (GACP)	Part II of the GMP Guide	Part I of the GMP Guide
Cultivation, collection and harvesting of plants, algae, fungi and lichens, and collection of exudates			
Cutting and drying of plants, algae, fungi and lichens, and exudates			
Expression from plants and distillation			
Comminution, processing of exudates, extraction from plants, fractionation, purification, concentration, or fermentation of herbal substances			
Further processing into a dosage form including packaging as medicinal product			

The transition between GACP and GMP can be seen as a relay run where the baton is given fromthe GACP to the GMP. The more the documentation and the GACP compliance is followed, the better streamlining between these two practices becomes. This will be the case especially if questions are raised by the regulatory agencies once a product is submitted. It becomes easily understandable that if all requirements are fulfilled from scratch, smoothly gaped and harmonized from GACP to GMP, then nothing will be left to chance. Furthermore, if a technical transfer is needed, for any reasons, this harmonization will smoothly scale-up too.

Another schematic representation like the above Table 1. is shown below where the emphasis onGMP is illustrated Figure 1. Represents below the different GACP/GMP steps to be followed, the gap junction between both and particularly the increasing GMP requirements that will be encountered down the road during product development.[9] The more a product is revised under the loop by a regulatory agency, such as a drug product, the smoother the transition between the GACP and the GMP will be. For this reason, it is highly recommended that a quality assurance (QA) audit be done on the whole GACP/GMP process, and the Standard Operating Procedures, or SOPs, be written and followed under the "pharmaceutical way of thinking", which is certainly more stringent but more rigorous and may narrow down pitfalls and questions from the plant's traceability down to the drug product.



Graphic 1: Progressive GACP/GMP to be followed for plant product development

In this short communication, the author tried to illustrate how GACPs and GMPs can be associated and should be streamlined, harmonized, to get the best quality product at the end.

GACPs should ensure that the native harvested plant, that will be formulated as a botanical drug product, will be traceable from its native seeds to the final drug product, under the supervision of both the GACPs and then the GMPs. Plant substances/extracts will then be released, not only according to their routine "certificates of analysis" but based on their full origin. The product development landscape is evolving, compounds generated more and more from plants and extracts. Also, to increase production efficiency, quality, and reproducibility as well as to narrow down the contamination and errors, the continuous manufacturing of drug substances and drug products,[10] will generate a production flow to reach these new standards of quality.

Botanical substances' quality will not only be determined by quality control but by their full traceability and in-process quality control tests. As mentioned, the more a plan product will require quality, such as natural health product or drug product, the better the GMP should drive the regulatory pathway to follow. Thus, the GACPs' SOPs should be written and build accordingly.

REFERENCES

1. https://clinicaltrials.gov/ct2/results?cond=&term=oral+insulin&cntry=&state=&city=&di st=
2. https://clinicaltrials.gov/ct2/show/NCT05067933
3. https://www.fda.gov/media/93113/download
4. https://database.ich.org/sites/default/files/Q7%20Guideline.pdf
5. https://database.ich.org/sites/default/files/Q8%28R2%29%20Guideline.pdf
6. https://www.ema.europa.eu/en/good-agricultural-collection-practice-starting-materials- herbal-origin
7. https://database.ich.org/sites/default/files/ICH_Q3C-R8_Guideline_Step4_2021_0422_1.pdf
8. PIC/S Annex 7. The transition from GACP vs GMP
9. GACP and GMP in the Medicinal Cannabis Industry- Cannabisscientech.com
10. https://database.ich.org/sites/default/files/ICH_Q13_Step2_DraftGuideline_%202021_07 27.pdf