CHAPTER 9

Summary and conclusion

The overall aim of this thesis is the evaluation and development of alternative visual inspection solutions based on the use of computer vision and deep learning to perform the quality control of parenteral products. This quality control often relies on human operators to verify the integrity of drug products in various forms, either lyophilised or liquid. It can be the inspection of particles from different origins or cosmetic defects that might present a risk for patients. Chapter 1 gives a short introduction to why innovation in manufacturing sciences is essential and why it would lead to higher product quality.

Chapter 2 introduced the fundamental concepts of freeze-drying. Additionally, the innovative technique called continuous spin freeze drying, developed by Rheavita, is introduced alongside its benefits compared to the traditional batch approach from a process and quality point of view but also regarding the unveiled potential for visual inspection considering the specific visual output of the product expected with this technology.

The fundamentals of visual inspection, the regulatory expectation and the prospect of machine vision solutions are discussed in Chapter 3. Traditional visual inspection, despite being effective to some extent, remains highly dependent on trained human operators, making it prone to errors caused by fatigue and inconsistencies. In contrast, the application of computer vision and deep learning introduced in Chapter 4 can revolutionise pharmaceutical quality control in both efficacy and efficiency. Additionally, this chapter demonstrates how AI offers the possibility of real-time process monitoring and adaptive control, which traditional methods struggle to achieve. By implementing AI and machine vision, the pharmaceutical industry can significantly reduce costs, enhance product quality, and ensure compliance with regulatory standards while adapting to the rising demand for automation and scalability in production.

The pharmaceutical industry is progressing towards more continuous manufacturing techniques. To dry biopharmaceuticals, continuous freeze drying has several advantages in manufacturing and process analytical control compared to batch freeze-drying, including better visual inspection potential. Visual inspection of freeze-dried products is a key quality control step to ensure that the products are free from foreign particles and defects. However, this process is labour-intensive, as operators must assess thousands of samples, leading to inherent inefficiencies. In Chapter 5, continuously freeze-dried samples were prepared based on a real-world pharmaceutical product using manually induced particles of different sizes and subsequently imaged using a tailor-made setup to develop an image dataset (with particle sizes from 50µm to 1mm) used to train multiple object detection models. You Only Look Once version 7 (YOLOv7) model outperformed human inspection by a large margin, obtaining particle detection precision of up to 88.9% while controlling the recall at 81.2%, thus detecting most of the object present in the images, with an inference time of less than 1 second per vial. This chapter demonstrated the potential of deep learning for particle detection in lyophilised products using specific foreign objects (e.g. fibres and perfect beads). However, the beads used in this work presented spherical shapes and known sizes, which may differ from real-world production conditions where foreign particles can vary significantly in size and shape. Therefore, a new model training would be required to adapt to different particle characteristics. Nevertheless, the particles used in this study provided valuable insight into the size range that the model can effectively detect.

Cosmetic inspection of freeze-dried products is an important part of the post-manufacturing quality control process. Traditionally done by human visual inspection, this method poses typical challenges and shortcomings that can be addressed with innovative techniques. In Chapter 6, several continuously freeze-dried samples were prepared using formulations and process settings that lead to the most recurrent defects encountered with this manufacturing technique. Two approaches capable of handling high-resolution images based on Convolutional Neural Networks were developed and compared towards the selection of the optimal one. Additional visualisation techniques were used to enhance model understanding further. The most efficient approach achieved perfect precision and recall on critical defects, with a prediction time of less than 50 milliseconds, enabling real-time decision-making on whether to accept or reject vials. However, the limited number of samples available for this study made it difficult to draw general conclusions. In addition, this work encompassed five specific defects that were created on purpose; thus, if a new defect

type were to be encountered, the model would need to be retrained to account for this new cosmetic anomaly.

In Chapter 7, the feasibility of an AI-driven visual inspection system for classifying particles within production vials was explored, with promising results. This chapter addressed industry challenges related to manual inspection limitations and slow analysis times. A model was developed by employing a specific computer vision approach and a supervised domain adaptation approach to classify particles as intrinsic or extrinsic, with F1 scores of 0.92 and 0.93, respectively. Despite a clear potential to improve visual inspection, several limitations were identified, mainly related to the type of acquisition hardware used and the insufficiency of representative data available. Nonetheless, this chapter further demonstrated the significant advantages of applying AI in the visual inspection area, with state of the art model reaching an accuracy of 85% given the classification in consideration.

Ultimately, in Chapter 8, the broader scope and future perspectives of the pharmaceutical industry were discussed. The chapter first explored the shift towards continuous manufacturing, followed by the trend of digitalisation, and finally, the increasing use of artificial intelligence in the manufacturing environment. In general, it can be concluded that AI has the potential to significantly revolutionise manufacturing processes by improving quality control, reducing cost, and enabling real-time decision-making, thereby positioning itself as a key driver of innovation in the pharmaceutical industry.