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CONTROL OF CRITICAL MATERIAL IN A GMP FACILITY FOR CELL AND TISSUE MANIPULATION - UKM MEDICAL CENTRE EXPERIENCE

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SUMMARY

Introduction: Tissue Engineering Centre has experience in managing and maintaining a GMP facility for almost 8 years. GMP guidelines require that the manufacturing of cells and tissue products for human use to be conducted in a controlled environment to ensure safety and efficacy of the product as regulated by the National Pharmaceutical Regulatory Agency (NPRA). Part of the system involves controlling the flow of critical materials into the facility. The process of critical material control includes verification inspection, use testing and material defect reporting. A system of 'Quarantined, Rejected, and Released' is implemented to help in the control process. Discussion: Critical materials are items that is deemed to have a direct or indirect effect on a product or service. This material is considered as critical and involves multiple process of checking, evaluating or use testing. The process of critical material receipt and verification is an important step in order to maintain a functional Quality System in a GMP facility. Conclusion: Being among the first to have such a facility, we hope that our experience can help other emerging GMP facilities as a reference centre.

1.0 Introduction

Tissue engineering involves multiple fields of regenerative medicine that aims to replace, repair or restore the normal function to diseased organs or tissue [1]. The advancements in the fields was made possible by the setting up of a Good Manufacturing Practice (GMP) facility for cell and tissue manipulation [2]. In order to ensure safety and quality is not jeopardized, all activity that is performed in the facility, ranging from sample collection, processing, testing, storage and product release must be performed in a controlled fashion to allow traceability[3]. Standard Operating Procedures (SOP) needs to be developed to maintain the standard associated with GMP [4]. One of the process involves in this is the control of critical material. Thus, this article is going to discuss on the experience of Tissue Engineering Centre in managing the GMP facility, particularly on various ways in controlling the flow of critical material into the facility, as well as the challenges encountered in making sure that the standards are not compromised, as per required by the National Pharmaceutical Regulatory Agency (NPRA).

2.0 Materials and Method

2.1 Critical Material Specification & Register

In the process of controlling the critical material, documentation is very important. A register was implemented and was made in use under the Quality System. In the event that there is a change to a particular material, the register must be updated.

2.2 Vendor Qualification

A register of vendors qualified for the supply of critical material must be implemented. Prior to their qualification, a vendor survey must be carried out to determine the suitability of the vendor. This might include a visit to the vendor's store house and cold chain monitoring system. Ideally, an agreement with the vendor should be signed by both parties to ensure mutual interests are met.

2.3 Receipt and processing of critical material

All item that arrived into the facility will be taken to the Pre-quarantine area for inspection and processing. All material need to be stored and kept according to its specific requirement. A system of 'Quarantined, Rejected and Released' was implemented to all item upon delivery. This system helps ensure that all item were inspected and documented properly.

2.4 Verification Inspection

Items will be inspected visually in accordance to the Critical Material Register and corresponding Material Specification. If the good meets the acceptance criteria, it will be released and allowed into the facility for use. Each batch of material will be inspected and tested for its functionality if necessary. During the testing of its functionality or when necessary document (certificate of analysis) is pending, the items are stored in appropriate storage temperature with a "Quarantined' label attached to the items. Only competent personnel familiar with the critical material acceptance criteria are allowed to release the products. For items to be released, the label 'Released" must be attached to the items with information such as the initial of personnel releasing, expiry date, batch / lot number, and date of items receipt clearly displayed on the label. Additional labels must be prepared for each item in a bulk packaging. Items that failed the acceptance criteria are label "Rejected" and to be stored away in preparation for their discard.

2.5 Use Testing

Use testing was performed on each batch of items which has specific function and activity. This includes items that contained enzymatic activity such as Collagenase. The test must be performed according to their respective SOP and recorded for future reference.

2.6 Traceability

The batch and lot of the critical materials assigned to specific batch of production must be recorded clearly in the production batch record. It is important to note that a batch number should be assigned to upon receipt of the critical material. Alternatively, batch number provided by the manufacturer along with the date of receipt is used to identify the exact batch of critical material.

The monitoring of the storage environment of the critical materials provided added assurance that the quality and function of these critical materials are not compromised at all times.

3.0 Discussion & Conclusion

Critical material are items that is deemed to have direct or indirect effect on the product or service. This material is considered as critical and involves multiple process of checking, evaluating or testing. Use testing must be performed on each batch of items which has specific function or activity, such as collagenase type I. their functionality must be tested prior usage in order to ensure that the items are in optimal condition, in accordance to its specification. The 'Quarantined, Rejected and Released' system is introduced in the management of the material through the verification process. Upon inspection, the item that meet the acceptance criteria will be label RELEASED (green label). If the material did not meet the acceptance criteria, a QUARANTINED or REJECTED label (yellow and red label respectively) will be pasted depending on the requirement needed. This colour coding system that is practiced is an effective exercise in maintaining the GMP standard. In order to have a smooth and working system, manufacturer and supplier also play a key role. Coordination between the personnel and the supplier is crucial to ensure that the GMP standards are not compromised. Thus, certain items that has short expiry date were arranged in such a way that they were delivered in a few batches among a certain period of time to ensure that the item reach the facility in its best condition. Specific requirements such as triple packaging for critical items were coordinated with the supplier. We find that this needs to be applied to items entering the facility to make sure that the level of cleanliness of the material is optimal. As certain items do not come in triple packaging, it is important to have a supplier or agent that can accommodate and help abide to this requirement. In conclusion, the process of critical material receipt and verification is an important step in order to maintain a functional Quality System. In the 8 years of experience and practice, we have been able to maintain an effective and functional critical material receipt and verification system that allows traceability. Being among the first to have such a facility without any national guidelines on cell and gene therapy when the facility was established, we hope that our experience can help other emerging GMP facilities as a reference center to have a better understanding in the process of control of critical materials.

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