IMP Manufacturer Vendor Assessment Process

Background

Under the principles of Good Clinical Practice, the sponsor is responsible for ensuring that a clinical trial is conducted in accordance with GCP and all other applicable regulations.

In the case of manufacture the sponsor is responsible for ensuring that all IMP are manufactured in accordance with current Good Manufacturing Practice (GMP). From a regulatory perspective, IMP manufacture must be compliant with Article 13 of Directive 2001/20/EC and Annex 13 and 16 of Eudralex Volume 4 which legislate for manufacture of IMPs and certification and batch release by a Qualified Person (QP). UK legislation on IMP manufacture is covered by part 6 and 7 of the Medicines for Human Use (Clinical Trial) Regulations 2004 (SI 2004/1031).

Whilst the sponsor may transfer trial related duties and functions to other organisations, the ultimate responsibility for quality and integrity of the clinical trial lies with the sponsor. The use of the IMP vendor assessment programme on a risk based approach is one element of ensuring that quality standards are met.

Defining manufacture

Within the UK legislation, manufacture of an investigational medicinal product (IMP) is defined as:

any process carried out in the course of making the product, but does not include dissolving or dispersing the product in, or diluting it or mixing it with, some other substance used as a vehicle for the purposes of administering it;

Manufacturing steps may include but are not limited to:

- manufacture of active IMP from active pharmaceutical ingredient(API)
- manufacture of placebo
- blinding for example by overencapsulation of a licensed medicine and preparation of a matched placebo
- packaging
- labelling
- final QP release certification of finished IMP
- import of IMP (has additional requirements)

Routes for manufacture of IMPs by NHS GG&C/Co-Sponsor

IMPs for use in a clinical trial are normally procured via the following methods:

- Use of site hospital stock
- IMP is provided by the Marketing Authorisation Holder (MAH) in UK livery with no additional manufacturing steps performed by the MAH.
- IMP is provided as study specific stock by a pharmaceutical industry partner. Responsibility for manufacture and/or final QP release is completed by the industry partner
- IMP is provided as study specific stock by a pharmaceutical industry partner. The industry partner then engages the services of a specialist IMP contract manufacturer to perform manufacturing steps and final QP release. In the latter case, the industry partner contracts with the IMP contract manufacturer. NHS GG&C are not party to the agreement.
- IMP is manufactured by a specialist IMP contract manufacturer engaged by the NHS GG&C/co-sponsor to manufacture IMPs in accordance with sponsor requirements. NHS GG&C are party to the agreement with the IMP contract manufacturer.

- An industry partner provides bulk stock with an intermediate QP release. NHS GG&C/co-sponsor are then required to engage the services of a specialist contract IMP manufacturer to undertake any remaining manufacturing steps and provide final QP release. In this instance the sponsor/co-sponsor will hold separate contracts with the industry partner and with the IMP contract manufacturer.

Risk management

In terms of risks to the IMP from manufacture there are two key factors which may potentially impact:

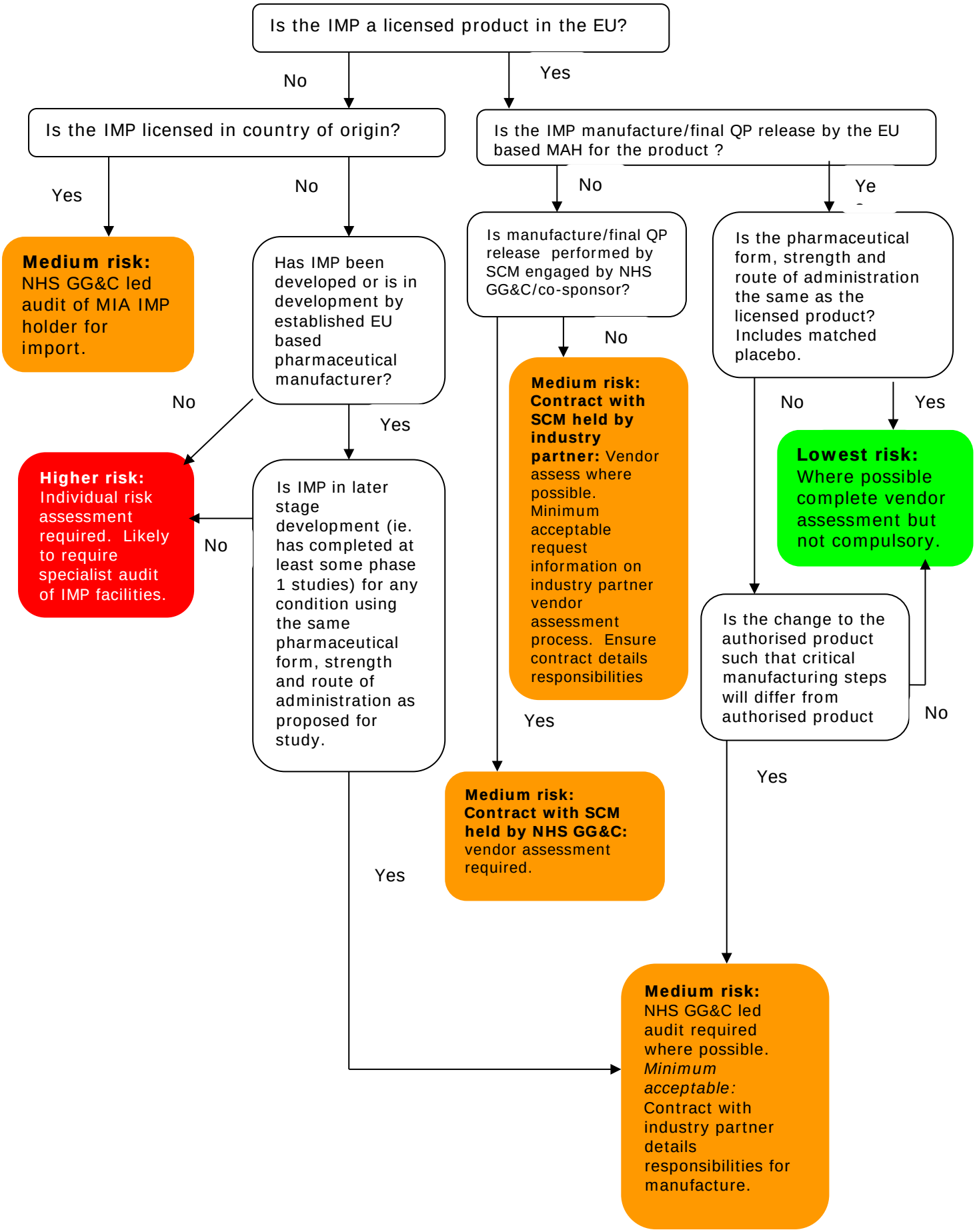
- route of manufacture
- potential risks associated with the IMP

Route of manufacture: The route of manufacture has a bearing on risk with contracted manufacture being of higher risk compared to manufacture by the MAH for the same product.

Risks associated with the IMP: Under the MHRA 'Risk Adapted Approaches to the Management of Clinical Trials of Investigative Medicinal Products' three types of trial are identified based on the potential risks associated with the IMP. Manufacture of novel IMPs particularly in early phase studies where there may be more limited information available are inherently of higher risk than manufacture of established products. Consequently the level of auditing required as part of NHS GG&C/co-sponsor should be commensurate with the anticipated level of risk. **Figure 1** provides a flow chart to guide the level of vendor assessment. The flow chart has limitations as it does not take into account for example the potential complexity of IMP manufacture or additional risks associated with sterile products for example. Experience over recent years indicates that large established pharmaceutical organisations can be to reticent to complete vendor assessments provided and that it is not always possible for NHS GG&C to be able to complete the desired level of vendor assessment. To cover such instances, some flexibility is included detailing the minimum acceptable standard. A SOP deviation form will be prepared where vendor assessment does not meet the minimum criteria detailed in the flow diagram.

Forms 51.15E Vendor assessment tool for IMP manufacturers and 51.15F Vendor Assessment Report provide a template audit tool and vendor assessment report respectively.

Figure 1: Flowchart summarising vendor assessment requirements



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Document History

Version	Details	Date
1.0	Version 1.0 creation	02/05/2013
2.0	Guideline renumbered	14/07/2016
3.0	Text amended to include further clarification on procurement routes for IMPS for studies sponsored/co-sponsored by NHS GG&C. Flow diagram revised Inclusion of Form 51.015E Vendor Assessment Report (Template)	12/12/2018