AIDE MEMOIRE FOR GMP INSPECTION OF MANUFACTURERS COMPLIANCE WITH COMMISSION DELEGATED REGULATION (EU) 2016/161 FOR SAFETY FEATURES

欧盟法令（EU）2016/161 安全特性的生产商符合性 GMP 检查备忘录

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Area of operations /items 项目	Questions/Show me 需要提问的问题/需要提供的资料	References(where applicable) 参考（如适用）
General 总体要求	Are all prescriptions products manufactured at the site required to bear safety features? 所有在工厂生产的处方产品是否需要具备安全特性？ Are any products exempted under Annex I? 是否有产品根据附录 1 获得豁免？ Are any OTC products required to bear safety features under Annex II? 是否有任何 OTC 产品根据附录 2 需要具备安全特性？ Are there products with different requirements in different EU Member States (e.g. prescription in certain MS & OTC in another)? 是否有不同欧盟成员国不同要求的产品(例如,某些 MS &OTC 中的产品)? If so, how is this handled? 如果是,如何处理? Is there a procedure or authorised listing available specifying which products are within the scope of the DR and specific requirements in the different Member States (if applicable)? 是否有规程或经批准的清单,具体说明哪些产品在 DR 的范围，以及不同成员国的具体要求(如适用)? Review deviation/non-conformance listings for any exceptional release of batches without safety features, after the 9 February 2019. Check for notification/authorisation by NCAs in this regard. 审核任何在 2019 年 2 月 9 日之后不具备安全特性的异常批次的偏差/不符合清单。检查 NCAs 在这方面的通知/授权。 Seek clarification regarding any batches released prior to the 9 February 2019 bearing safety features. Has this data been uploaded? 请澄清 2019 年 2 月 9 日之前放行的任何包含安全特性的批次。这些数据上传了吗? Are products imported from India and certified at the site? 产品是从印度进口的,并在现场获得认证? If so, has the company notified its CMO in India of the requirements of the Delegated Regulation and to request that the CMO seeks an exemption from the Indian Authorities in relation to the Indian traceability system, so that these Indian barcodes are no longer applied to packs exported to the EU?	Article 9 DR

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	如果是,公司是否通知其在印度的 CMO,要求 CMO 就印度可追溯性系统向印度当局申请豁免,以便不再应用这些印度条形码以包装出口到欧盟?	
Connection with the Hub 与欧盟中心的连接	Who is the On-Boarding Partner (OBP) and where is this entity located? 谁是 OBP 以及此实体位于何处? Show me the agreement between the OBP and EMVO? 提供 OBP 与 EMVO 之间的协议? Where the OBP is not the manufacturer, request to see the agreement/contract between the manufacturer and OBP outlining responsibilities of the parties. 如果 OBP 不是制造商，提供制造商与 OBP 之间的协议/合同,概述各方的责任。 Are the responsibilities regarding the UI/ATD stipulated in an agreement/contract with the MAH? 是否在与 MAH 签订的协议/合同中规定有关 UI/ATD 的责任? Do the contracts cover at a minimum responsibilities for the following: 合同至少包括以下责任: - Management of Product Master Data in the Hub 欧盟中心中产品主数据的管理 - The generation of SN's SN 的生成 - The upload of data into the hub 数据上传至中心 - Status changes to UIs to Recalled, Stolen, etc. 状态变更为“已召回”、“被盗”等 - The immediate investigation and communication of a suspected falsified pack, based on an alert in the EMVS? 根据 EMVS 中的警报,立即调查和通报涉嫌伪造的包装。	EU GMP Guide, Part I, Chapter 7
Registration with the NMVOs 在 NMVO 注册	Where the manufacturer is also the MAH, has it registered with all relevant NMVOs? 如果制造商也是 MAH,是否已在所有相关的 NMVOs 上注册?	
Data Flow 数据流	How does the batch data (serialisation numbers) get to the hub from the site of manufacture? 批数据(序列化编号)如何从制造站点传送至中心? Show me the system description, data flow and interfaces with other systems? 提供系统描述、数据流和与其他系统的接口? Data-flow from:	EU GMP Guide, Part I, Annex 11, Principle & Paragraph 4; EU GMP Guide, Part I, Chapter 7

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	数据流包括： - where the SN's are generated 何处生成 SN - to where the UIs are printed on the packaging-line 何处将 UI 打印至包装线上 - to the hub where the UIs are uploaded 何处将 UI 上传至中心 Are all entities involved identified along the chain of flow of data? 是否所有涉及的实体已沿着数据流链条确定? Who is the sites contracted serialisation partner? 谁是工厂签约的序列化合作伙伴 Show me the ISO 27001 Information Security Management System Certificate of Registration for this serialisation partner. 提供此序列化合作伙伴的 ISO 27001 信息安全管理系统的认证证书。 Is the system a Cloud Based system and where are the servers located (e.g. US)? 系统是否为基于云的系统,服务器位于何处(例如美国)? Has an audit been carried out to assess the quality of the serialisation partner's quality management system and hosted cloud environment? 是否已对序列化合作伙伴进行审计以评估的质量管理体系和云环境的质量? Is there a Gateway Provider involved? 是否涉及网关提供程序? If yes, who is the gateway provider? 如果是,谁是网关提供商? Has this service provider been qualified? 此服务提供商是否已确认? What knowledge do you have about the service provider's quality management system? 你对服务提供商的质量管理体系了解如何? Has a security audit/assessment been conducted? 是否已进行安全审计/评估? Show me the audit reports/assessment reports	PIC/S Guide PI 011-3, Section 11 (IT Service supplier qualification) Q&A COM 7.19

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	提供审计报告/评估报告 Are responsibilities defined in Quality/Technical Agreements/Contracts between all relevant parties involved in the chain of data flow? 是否已在质量/技术协议/合同中明确所有涉及数据流链条的相关方之间的责任？ What additional software has been installed at the site for the purpose of serialisation and compliance with the DR? 为了序列化和符合 DR,现场还安装了哪些其他软件? Where there are interfaces between the company's serialisation system and other systems (e.g. MES, ERP), do these other systems store or transfer the data (e.g. PC, SN)? 如果公司的序列化系统与其他系统(例如 MES、ERP)之间存在接口,这些其他系统是否存储或传输数据(例如 PC、SN)? Has the software been validated, including any inter- connections (e.g. no alteration to uploaded data: expiry date, capital letters vs. lower case etc.)? 软件是否经过验证,包括任何相互连接(例如,对上传的数据不作任何更改:有效期、大写字母与小写等)? Is there a risk based audit trail review of the operations executed within the serialisation system? 是否对序列化系统内执行的操作进行基于风险的审计追踪审核?	
Generation of Serial Numbers (SNs) 序列码的产生	Where/by whom are the SNs generated? Is there a Contract in place? 在哪里/谁生成了序列码？是否有合同？ Is it generated by a deterministic or a non- deterministic randomisation algorithm, in a way that the probability that the serial number can be guessed shall be negligible and in any case lower than one in ten thousand? 它是由确定性或非确定性随机化算法生成的,可猜到序列号的概率可以忽略不计,并且在任何情况下都低于万分之一? Is the combination of the PC+SN unique until EXP+1Y or REL+5Y, whichever is the longer period? PC+SN 的组合在有效期后一年（ EXP+1Y） 或五年（ REL=5Y）（以较长的周期为准） 之前是否唯一? Is serialisation data received from other parties, e.g. CMO's? If yes, how (e.g. connection with the CMO's system)? 是否从其他方(例如 CMO)接收序列化数据?如果是,如何接收？(例如：如何	Articles 4b (ii), 4c DR Article 4d DR

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	与 CMO 的系统连接)? Has the security of the connection been evaluated? 连接的安全性是否已评估? Who manages/controls the Product Master Data in the hub (e.g. creation of a new product, changes to an existing product)? 谁管理/控制中心中的主数据(例如,创建新产品、对现有产品的更改)? How is it ensured that only Product Master Data from legitimate marketed packs is uploaded? 如何确保仅上传合法销售包中的产品主数据? (i.e. once a company passes EMVO's legitimacy check and gets access, how is that company prevented from creating non-existing products in the system and upload of SN's for t his fake product, to enable distribution of falsified product) (例如,一旦公司通过 EMVO 的合法性检查并获得访问权限,该公司如何阻止在系统中创建不存在的产品并上传假冒产品 SN)	
Uploading of information in the repositories system 在存储库系统中上传信息	At what point in the batch release process is the data uploaded? 在批放行过程中的什么节点上传数据? Is the data sent to the serialisation partner's server first and held for a period or stored temporarily in the manufacturer's/MAH's cloud, prior to upload to the hub? 在上传到数据中心之前，数据是否首先发送到序列化合作伙伴的服务器,并暂存一段时间或暂存在生产企业/MAH 的云服务器中? How is the upload to the hub actually triggered? 如何触发上传到数据中心? How is it ensured that only the data for 'good' packs (suitable for release) is uploaded to the hub? 如何确保只有"好的"包装(可放行)的数据上传到数据中心? Is the system designed in a way that no upload of data goes undetected/that any upload of data requires approval (of the QP?) before actually sending it to the hub? 系统的设计方式是否是：数据不会未经检测即上传/即任何数据上传都需要（经过 QP）批准? What happens to the UIs which were generated but not used and UIs on packs ejected from the line at the eject stations during packaging?	Article 33 DR COM Q&A 8.6 COM Q&A 7.16

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	如何处理已生成但未使用的 UIs 和在包装过程被从生产线剔除的包装上的 UIs? Is a verification of successful upload and distribution required to be obtained? 是否需要验证成功上传和分发? Is it verified whether the quantity of serial numbers successfully received by the NMVS, corresponds to the quantity of serial numbers that was initially intended to be uploaded (reconciliation of the number of SN's)? 是否验证 NMVS 成功接收的序列码的数量是否与最初上传的序列码数量一致(SN 编码的物料平衡)? Who receives this and what action is required in the event of a failed upload? 谁收到此内容，上传失败时需要执行采取什么措施? Does the (successful) upload occur before or after batch certification by the QP? (成功)上传是在 QP 的批放行之前还是之后? Does the (successful) upload happen before or after release to the market or for export? (成功)上传是在放行上市/放行出口之前还是之后? Are there procedures which describe these processes? 是否有描述这些流程的文件? (Note: The information laid down in Article 33(2) of Commission Delegated Regulation (EU) 2016/161 needs to be present in the system at the time the batch is released for sale and distribution) (注:2016/161 年《委员会委托条例》(EU)第 33(2)条中规定，在放行销售和分销时，信息需要存在于系统中)	
Packaging Lines 包装线	Was serialisation for EU implemented at the site under change control? 欧盟序列化在变更控制下实施吗? Did this change control process include identification of QMS documentation which required update to incorporate safety features? (e.g. procedures for recall, quality defects, batch disposition, shipment, distribution etc.; batch records, job descriptions for key personnel/QP, technical/quality agreements) 此变更控制流程是否包括需要更新以纳入安全功能的 QMS 文件的标识?(例如召回程序、质量缺陷、批次处置、装运、分销等;批记录、关键人员/QP 的岗位说明、技术/质量协议)	EU GMP Guide, Part I, Annex 15 Article 5.3 DR COM Q&A 2.21 Article 14 DR

Area of operations /items 项目	Questions/Show me 需要提问的问题/需要提供的资料	References(where applicable) 参考（如适用）
	Are both the 2D barcode and the ATD applied? 二维码和 ATD 都应用了吗? In the case of the ATD, get the company to demonstrate that if removed or broken, this is evident visually from the pack. ATD 让公司可以从包装上明显的看出开封或损坏。 Is stability data available? (Tamper evident nature should be proven throughout the shelf life of the pack) 稳定性数据是否可用?(在包装的效期内应开盒可留痕) Which packaging lines have capability for serialisation? 哪些包装生产线具有序列化功能? Was new equipment installed and was it qualified? (e.g. printers, cameras, reject stations etc.). 新设备安装后是否经设备验证?(例如打印机、摄像头、剔除等)。 Review change control, qualification documentation etc. 审核变更控制、设备确认文件等 Is the UI printed on the packs online or are labels/stickers applied to packs separately? UI 是在线打印在包装上，还是将标签/标签分开贴在包装上? Is there 100% verification of the readability of the 2D barcode? How is this done (e.g. on-line camera)? 二维码的可读性是否 100%确认?这是如何做到的(例如在线摄像机)? Is there an on-line sensor to detect the presence of ATDs and is it challenged? 是否有在线探头来检测是否存在 ATD，是否有挑战? Is aggregation implemented? 是否关联? Explain how (e.g. UI's in 1 data-file. What happens with the data-file. How is this protected/transferred in a secure way)? 说明如何关联(例如 UI 关联到 1 个数据文件中，数据文件会发生什么情况。如何以安全的方式保护/传输?)	
Composition of the UI UI 的组成	Does it consist of the required data elements? 它是否包括所需的数据元素?	Article 4 DR QRD Templates Appendix II

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	-Product code (max 50 letters or numbers),allowing the ID of the name & common name of the product, pharmaceutical form, strength, pack size, pack type, optional: info regarding reimbursement Should be printed on the pack, preceded by the letters PC -产品代码(最多 50 个字母或数字)，允许产品名&产品通用名的的 ID，产品剂型，规格，包装尺寸，包装形式。可选:有关报销的信息 应打印在包装上,前面是字母 PC - Serial n° (max 20 letters or numbers) Should be printed on the pack preceded by the letters SN 序列码 n* (最多 20 个字母或数字) 应打印在包装上,前面有字母 SN - Expiry date Should be printed on the pack by EXP (Note: The word “EXP” is not in use in all Member States. Country specific words may be used) - 失效期 应使用失效期的形式在包装上打印(注:并非所有成员国都使用"EXP"一词)。可使用特定于国家/地区的词语) - Batch number Should be printed on the pack by LOT (Note: The word “LOT ” is not in use in all Member States. Country specific words may be used) - 批号 应按 LOT 在包装上打印(注:并非所有成员国都使用"LOT"一词)。可使用特定于国家/地区的词语) How is the PC managed in the quality system? Who is responsible for its generation/management? What is its format (e.g. GTIN/NTIN)? 在质量系统中如何管理 PC? 谁负责它的生成/管理?是什么格式(例如 GTIN/NTIN)?	Section 18
Human-readable format 人可读格式	Are the following data elements on the packaging in human-readable format: (a) the product code (b) the serial number (c) the national reimbursement number, if required The batch number and expiry date should also be on the packaging in human readable format. 包装上的以下数据元素是否为人可读格式: (a)产品代码 (b)序列号 (c)国家报销号，如需	Article 7 DR

Area of operations /items 项目	Questions/Show me 需要提问的问题/需要提供的资料	References(where applicable) 参考（如适用）
	批号和失效期也应以人可读格式出现在包装上。	
Quality of the printing of the 2D barcode 二维码打印质量	Has the manufacturer evaluated the quality of the printing by assessing the following parameters: (a) the contrast between the light and dark parts (b) the uniformity of the reflectance of the light and dark parts (c) the axial non-uniformity (d) the grid non-uniformity (e) the unused error correction (f) the fixed pattern damage (g) the capacity of the reference decode algorithm to decode the Data Matrix. 生产企业通过评估以下参数来评估打印质量: (a) 明暗部分之间的对比度 (b) 明暗部分反射的均匀性 (c) 轴向非均匀性 (d) 网格非均匀性 (e)未使用纠错 (f)固定模式损坏 (g)参考解码算法的容量解码数据矩阵。 How was this performed? If a dedicated equipment is installed for this purpose, is it qualified, is it included on the calibration/maintenance master plan etc.? 如何执行的? 如果为此目的安装了专用设备，是否经验证，是否包括在校准/保养总计划中等?	Article 6 DR
	Is the minimum quality of printing identified that ensures the reading of the Data Matrix for EXP-date +1Y, or REL-date +5Y, whichever is the longer period? (Not required when it is demonstrated that the Quality of Printing is at least 1,5 if in accordance with ISO15415:2011) 数据矩阵的最低打印质量是否可确保在失效日期+1 年或实际日期 +5 年(以较长时间段为准)期间数据矩阵是可读的?(如果根据 ISO15415:2011 证明打印质量至少为 1,5,则不需要)	
Reversing the status of a decommissioned UI 撤销已停用 UI 的状态	Is there a procedure in place for the reversal of the status of UI? 是否有文件规定撤销 UI 的状态	Article 13 DR
Record keeping 记录保存	Are records kept of the operations that are performed with or on the UI until EXP+1Y, or REL+5Y, whichever is the longer period?	Article 15 DR

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	Are these records available to the NCA? Are these records reviewed and approved? By whom? 在 EXP+1Y 或 REL=5Y(以较长时间段为准)之前,是否保留使用 UI 执行的操作的记录? 这些记录 NCA 能获取到吗? 这些记录是经过审核和批准的吗?谁批准/审核?	
Removing or replacing safety features 移除或替换安全功能	Are repackaging activities carried out? 是否执行重新包装操作？ If yes: are the SF's verified before the repackaging activity? 若是，安全功能在重新包装活动开始之前是否经确认？ Is the status of the "old" UI decommissioned? 旧的 UI 码的状态停用吗？ To what status? 到什么状态？ Can you demonstrate the equivalence between the old and the new ATD? 你能证明新旧 ATD 之间的等效性吗? Do you have SOP's that describe this? 是否有相关的 SOP 进行规定？	Articles 16 & 17 DR
Returns 退货	Is the UI verified for returns of medicinal products? 退货的药品是否进行 UI 确认？ Is this requirement included in a procedure? 此要求是否有文件规定？ Are records maintained? 是否保留相关记录？	Articles 19, 20 (a)
Decommissioning of unique identifiers 停用唯一标识符	Are UIs verified and decommissioned for the following: (a) products distributed outside the EU (b) returns which cannot be returned to saleable stock (c) products intended for destruction (d) products requested as samples by NCAs (e) products distributed to persons or institutions referred to in Article 23, where required by national legislation UIS 是否因下列原因得到验证和停用: (a) 在欧盟以外分销的产品 (b) 无法退回至可销售的退货 (c) 需要销毁的产品	Articles 22, 23 DR

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	(d) 作为 NCA (e)需求的样品的产品 (e) 根据国家法规要求，分发至第 23 条所述的个人或机构的产品 Are the above requirements included in a procedure? 以上要求是否有文件规定？ Are stock management/distribution systems configured to meet these requirements for the Article 23 entities? Has the process been qualified? 库存管理/分配系统配置是否符合法案第 23 章所列机构的要求?该流程是否经确认?	
	For holders of a compounding manufacturer's authorisation (these authorisation-holders may use commercially available product for unit-dosing or for compounding patient/prescription specific medicines for an individual patient) are the responsibilities for decommissioning defined? 对于复合生产的许可持有人(这些许可持有人可能将商业产品单剂使用或用于复方患者/单个患者的特定处方药物)，是否有职责定义停用?	
UI status change UI 状态变更	What status changes can the manufacturer perform on a pack/on a batch/on the product (e.g. Recalled, Withdrawn, Intended for Destruction, Stolen, Requested as a Sample by NCA)? . 生产企业可以在包装/批次/产品上执行哪些状态更改(例如,召回、撤回、打算销毁、被盗、NCA 需求样品)? When the status of a UI is changed to for e.g. Stolen, Recalled, Withdrawn or Locked by the MAH, does the manufacturer receive a message of this through the IT-system? 当 UI 的状态更改为"被盗"，被 MAH 召回或锁定，生产企业是否会通过 IT 系统收到此消息?	Articles 36b,36m DR
	Does the manufacturer get information on the status of a UI (e.g. Decommissioned, Recalled, Withdrawn, Intended for Destruction, Stolen, Requested as a Sample by NCA, Indicated as Free Sample by the MAH) when he verifies the authenticity of the UI? 生产企业在验证 UI 的真实性时，能否获取有关 UI 状态的信息(例如,停用、召回、撤回、打算销毁、被盗、NCA 需求样品、MAH 指定的免费样本)?	Article 36m DR
	Can a combination of a PC + SN of an old pack be removed from the EMVS, in order to upload a PC + SN of a new pack? 能否从 EMVS 中删除旧包装的 PC+SN 码的组合，以便上载新包装的 PC + SN 码?	Article 42 DR
Actions to be taken in case of tampering or	Show me the procedures describing actions to be taken in cases of tampering or suspected falsification. 展示描述在篡改或涉嫌伪造的情况下应采取的行动的文件。	Articles 18, 24 37d DR

Area of operations /items 项目	Questions/Show me 需要提问的问题/需要提供的资料	References(where applicable) 参考（如适用）
suspected falsification 在篡改或涉嫌伪造的情况下应采取的措施	Do procedures state that the manufacturer shall not release the product for sale or distribution and shall immediately inform the relevant competent authorities in the case of a confirmed falsification event, when technical/procedural root causes have been ruled out? 文件是否规定，若发生技术/程序根本原因已确定的确认的伪造事件。制造商不得将产品放行销售或分销，应立即通知相关主管当局?	
Alert Management 警报管理	Are alerts of potential falsification, generated by the EMVS on products manufactured at the site, notified to the site? How does this happen in practice? EMVS 对生产厂的产品发出的潜在伪造警报会通知生产厂吗？实际情况如何操作? Is there an SOP on the handling and investigation of such an alert, to determine whether the root cause is a technical or procedural issue? 是否有关于处理和调查此类警报的 SOP，以确定根本原因是技术问题还是程序问题?	Article 37d DR
Operations specific to Parallel Importers & Distributors 进口商和分销商并行的特定操作	Has the equivalence of the new ATD & UI placed on the packs with the original UI/ATD been assessed? How was this conducted? 新的 ATD & UI 与原 UI/ATD 的等效性已评估过吗?如何进行? Show me an example of how equivalence has been demonstrated. 提供一个示例,说明如何证实等效性。 Is the authenticity of the safety features on the sourced pack verified before unpacking? 在拆包前,是否验证了原包装上安全功能的真实性? Is the parallel repackaging functionality in the EUHub used when repackaging? 重新打包时是否使用了 EU Hub 中的并行重新包装功能? Explain how you deal with the following situations: 解释如何处理以下情况: - Sourcing packs from a country where the product is in scope of the DR, but not in scope in the target market? 从产品在 DR 范围内但并非目标市场范围内的国家/地区采购包装? - Sourcing packs from a country where the product is not in scope of the DR, but is in scope of the DR in the target market? 是否从产品不在 DR 范围内但位于目标市场 DR 范围内的国家/地区采购	Article 17 DR Q&A COM 1.22 2001/83/EC Art 47a (1)a

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	包装? If the patient information leaflet is replaced, are the packs re-boxed (i.e. new cartons) or are the original cartons resealed (e.g. by applying a new ATD on top of the old, broken ATD)? 如果更换了患者信息单,包装是重新装箱的(即新纸箱)还是重新密封原始纸箱(例如,在旧的、破碎的 ATD 上应用新的 ATD)? If the original cartons are resealed, has this been notified to the NCA in the destination Member State for assessment? 如果原纸箱被重新密封,是否将此通知目的地成员国的 NCA 进行评估?	