Health Institution Exemption
Draft MHRA guidance

Thank you for reviewing this draft guidance. In order to capture all of your comments, please use this template for your response. We have asked some specific questions in the text. They have been reproduced here to record your response.

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At the end of this document is a template for specific text changes.

Name	Engineering Policy & Standards Panel
Organisation	Institute of Physics & Engineering in Medicine (IPEM)
Date	March 2019

General Overall Comment

There is a public health need for greater controls of health institution in-house production and use of medical devices in order to ensure acceptable levels of patient safety and device performance and quality. Whilst this has been recognised in the new MD and IVD Regulations, (ie: the HI exemptions introduce conditions that were non-existent in the Directives, and the note in recital 28 of the IVD Regs.), the MHRA guidance on the HIE will be a critical determinant of the effectiveness with which the new requirements are applied across the health service.

Meeting the need for greater controls and oversight of in-house production and use of medical devices within health institutions should also be a positive factor in promoting medical device innovation within the health service. For example, to quote from the FDA *Laboratory Developed Tests* document (as referenced in Question-K below) ....
"While excessive oversight can discourage innovation, inadequate and inconsistent oversight ..... can also discourage innovation by making it difficult for high-quality ..... developers to compete with poorer performing counterparts."
This is true of development of medical devices generally, (not just diagnostic tests that are the subject of the quote), and is especially relevant in the health service. If the HIE guidance is not sufficiently robust, not only will poor practices persist, but good practices will continue to be compromised, (by managerial benchmarking against poor practices which appear 'acceptable' at lower effort and cost). Thus – contrary to claims often made – it is weak requirements, rather than robust requirements, that ultimately actually stifle innovation – because if necessary requirements are not clearly understood and appreciated then innovation does not get properly resourced to meet them.

In particular, critical aspects of the HIE warranting firm stipulation will be areas such as -
– health institution registration, oversight & enforcement;
– quality systems & technical documentation;
– Responsible Persons within health institutions;
– ongoing surveillance.

IPEM would therefore appeal for the MHRA guidance to establish minimum standards,

consistent with the intent of the Regulations, the satisfaction of which would be proportionate to risks involved with each particular product (as per the EN 13485 risk-proportionate approach).

Following publication of this guidance we recommend the issue of a NHS Patient Safety Alert (analogous to the alert NHS/PSA/D/2014/006 which mandated the establishment of medical device groups and Medical Device Safety Officers within HIs).
Publication of HIE guidance may pass unnoticed by some, but the issue of a NHS PSA would ensure that it is brought to the attention of every HI management board, and be a means of setting timelines for organisations to achieve HI compliance with the HIE guidance.

Once this guidance is published it would be useful to organise a meeting / Q&A session to share ideas on implementation.

Definitions and scope

QUESTION A	
Some examples of what we consider to be health institutions are obvious eg NHS Trusts/ NHS Boards, but what about the following?	
a) Collaborations led by a health institutions to provide healthcare?	Yes/No (see comments)
b) Collaborations led by a health institutions for product development with/without commercial intent?	Yes/No (see comments)
c) Free standing commercial laboratories?	No
Any other examples?	

GENERAL COMMENTS -

<u>Collaboration:</u>
- The intended meaning of 'collaboration' here may warrant elaboration.

<u>Healthcare Institution:</u>
- It should be made clear that a distributed healthcare organisation, that for example comprises numerous hospitals and premises but all having the same top level management Board, can be considered as a single Health Institution.

<u>Private Sector</u>:
- The distinction between public & private healthcare is increasingly blurred.
- But, if a private sector organisation builds a device for in-house use only, but then charges patients for healthcare services that use the device, has it not effectively been commercialised (placed on the market)? - In which case can it be acceptable to allow the exemption in the private sector?
- As such, the HI exemption should only be applicable to 'not-for-profit' organisations / activities.
- Whilst 5.5(a) of the exemption talks in terms of devices transferred between legal entities, note that the definition of 'making available on the market' (Article 2(27)) regards this as use '… in the course of a commercial activity'.

(Note - it is a little puzzling that although 'making *available on the market*' and '*placing on the market'* have separate definitions [MDR 27 and 28, IVDR 20 and 21 respectively), it is only '*placing on the market*' or '*putting into service'* that requires '*compliance with this Regulation'* [MDR Article 5.1]. MDR Recital (3) says that … *'This Regulation does not seek to harmonise rules relating to the further making available on the market of medical devices after they have already been put into service such as in the context of second-hand sales*.' … So, would it be legal to manufacture and put into service a device in-house [MDR Article 5.4 and 5.5], then *'make it available on the market'* as a second-hand device without complying with the Regulation? Is this a loop-hole?)

SPECIFIC QUESTIONS ABOVE:

a) Collaborations led by a health institutions to provide healthcare?

- Collaborations between HI and other HIs –

Without commercial intent –
– YES, HIE allowed - provided that one HI leads, has authority and takes responsibility.
With commercial intent –
– NO - If there is commercial intent then HIE is not applicable, the MDR/IVDR apply.
– If a device is initially developed without commercial intent under the HIE, but commercial value is subsequently identified, then the MDR/IVDR apply as soon as commercial intent arises.

- Collaborations between HI and non-commercial organisations (eg: academia, charities, 'not-for-profit' organisations, etc.) –

Without commercial intent –
– YES, HIE allowed - provided that HI leads, has authority and takes responsibility.
With commercial intent –
– NO - If there is commercial intent then HIE is not applicable, the MDR/IVDR apply.
– If a device is initially developed without commercial intent under the HIE, but commercial value is subsequently identified, then the MDR/IVDR apply as soon as commercial intent arises.

- Collaborations between HI and commercial organisations –

– NO, HIE not allowed.

b) Collaborations led by a health institutions for product development with/without commercial intent?

- Collaborations between HI and other HIs –

Without commercial intent –
– YES, HIE allowed - provided that one HI leads, has authority and takes responsibility.
With commercial intent –
– NO - If there is commercial intent then HIE is not applicable, the MDR/IVDR apply.
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- Collaborations between HI and non-commercial organisations (eg: academia, charities, 'not-for-profit' organisations, etc.) –

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– YES, HIE allowed - provided that HI leads, has authority and takes responsibility.
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– NO - If there is commercial intent then HIE is not applicable, the MDR/IVDR apply.
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commercial value is subsequently identified, then the MDR/IVDR apply as soon as commercial intent arises.

- Collaborations between HI and commercial organisations –

– NO, HIE not allowed.

(Note: Sub-contracting is not commercial collaboration, eg: If a HI developing a medical device sub-contracts the manufacture of a component to a commercial provider (because they don't have the in-house capability to do so), then that provider is managed as a sub-contractor within the HI's quality system – the provider is not a collaborator merely supplier of goods to the HI.)

c) Free standing commercial laboratories?

- Such commercial organisations could range from an embedded service within a single HI, to independent services providing to multiple clients.
  Such commercial organisations could provide services to HIs or direct to 'consumers'.

– NO, HIE not allowed - see the note on Private Sector above.

OTHER EXAMPLES

- GP or other healthcare professional services

– Not unless they are obliged to have a responsible person available expert in regulatory compliance,
– With regard Private Sector, see note above.

- A department within a legal entity (eg a laboratory or a MRI suite in a university) -

– It would need to satisfy the definition of Health Institution in the Regulations' recitals, and the device only used within that department

- The whole of the NHS?

It would be very desirable to be able to share within the NHS as a 'single entity', if it could be justified legally. (The need for this is evidenced by previous survey, which revealed the significant extent to which sharing of in-house produced devices across organisational boundaries within the NHS already exists.) However, considerations would be -

– The UK NHS is in four parts anyway, and within these are various divisions, NHS Trusts, Foundation Trusts, etc. – so it is difficult to see how 'the whole of the NHS' can be considered a single health institution.
– Legal justification may be problematical? Also, commercial organisations might challenge as unfair?
– With the exception of software devices, provision of devices by a HI to other HIs will incur additional production costs. As such, 'sharing' of devices between HIs will commonly not be for free – generally the originating HI will need to charge, (materials, resources, overheads, support, etc.) for supplying devices even if on a 'not-for-profit' basis; - it may be difficult to determine whether costs for supplying devices include profit.
– It is likely be difficult for the receiving HI assure the degree of compliance of the manufacturing HI against the HIE requirements.
– If not justifiable, then CE-marking will be required to exchange devices between NHS organisations - potentially stifling sharing and patient benefits, because some organisations will have the capacity / competency for in-house development whilst others will not.

(For example –
The NHS Wales Information Service (NWIS), hosted by one Trust but serving all NHS Wales, develops software applications to support organisations across NHS Wales; they are apparently having to plan for CE marking of products. Similarly, the Artificial Limb and Appliance Service in Wales is hosted by the Cardiff

Health Board but provides services throughout Wales. Regional services such as critical-care patient recovery / transfer operate across many hospital organisations. Etc,. etc.. The concept of shared clinical services between different Trusts / Health Boards / CCGs exists in NHS England also. Generally, NHS organisations are increasingly deploying services beyond traditional hospital / community boundaries as encouraged by the NHS transformation plans, creating wider NHS groupings (such as integrated care systems).

Performance studies and clinical investigations

QUESTION B	
a) Is this a right approach to the regulation of devices in clinical investigations and performance studies?	Yes/No (see comments)
b) Is this approach proportionate and desirable?	Yes/No (see comments)
c) What is an appropriate QMS for use in a clinical investigation/performance study?	
Please specify.	13485
d) Should clinical investigations/performance studies:	
Be registered with MHRA?	No
Comply with relevant GSPR?	Yes
Have the same level of justification?	Yes
e) Do general principles apply to performance studies (IVDR Article 57) and 'other clinical investigations' (MDR Article 82) when applying the exemption?	
IVDR Article 57	Yes
MDR Article 82	Yes
f) Any other comments?	

Questions (a) and (b)
See notes below.

Question (c)
Clinical investigations / performance studies are a component of the overall development of a medical device; this component does not require a QMS particular to it - rather, any HI producing in-house medical devices must be doing so within the overall 'appropriate' medical devices development quality system, as per requirements of the HIE (MDR/IVDR Article 5.5(b)) – clinical investigations and performance studies would be managed within that overall QMS. Within that QMS the appropriate standards ISO 14155 and ISO 20916 can be applied, for clinical investigations and performance studies respectively.
To be 'appropriate' the overall QMS should meet the QMS requirements of Articles MDR 10.9 / IVDR 10.8, (with due allowance for any non-applicabilities under the HIE). The most suitable way of achieving this is to apply EN 13485 quality system standard.
The use of EN 15189 as an appropriate QMS is problematical – see the notes below made against Page 12 of the draft.

Question (d)
Devices with commercial intent will fall outside of the HIE and so be subject to the general MDR/IVDR.
For devices without commercial intent under HIE, this is a more complex issue. Also an additional HIE challenge is that many researchers are not familiar with quality management systems, the GSPRs or relevant Standards and do not seek the appropriate advice for medical device studies that they should.

- YES - compliance with all applicable GSPRs, (except those aspect/s specifically identified as the purpose of the clinical investigation / performance study). GSPR applicability and compliance should be being assessed and addressed anyhow, from the original initiation and onwards throughout device design and development process.
- YES – the general principles for clinical / performance evaluation (including

investigations / studies) should apply to HIE devices.

- NO - MHRA registering of clinical investigations / performance studies should not be required under the HIE; the current cost of doing so would be prohibitive for most HIE projects, and would be an unfair cost burden on projects that have no commercial intent.
  (Unless the MHRA is able / willing to waiver the charges for registration of investigations / studies when they are HIE and hence with no commercial intent – in which case no-cost registration could be advantageous in providing for a level of transparency and independent oversight / surveillance. If the development of the device is being undertaken according to the HIE requirements of Article 5.5, then the information needed for MHRA registration should be readily available, so this should not be an onerous requirement.)
- NO - Even if the decision is to require MHRA registration of HIE clinical investigations / performance studies, the MHRA registering of early-stage 'proof of concept' studies should not be required, (i.e.: studies at the very early stages of the development of a device before a formal clinical investigation / performance study is appropriate). However this allowance would need careful definition in the HIE guidance, The judgement to be made will be at what stage of the device development does its preliminary evaluation of concept (not requiring MHRA notification) transition to a clinical investigation / performance study (which should require MHRA notification). This would warrant some elaboration in the HIE guidance. Also there would need to be clear labelling and control measures to ensure that devices in such early studies cannot be mistakenly (or wilfully) used for medical purposes.
  (The note above regarding lack of researcher awareness is still applicable at these early stages – but at least now, under the new legislation, they should be subject to the HIE device development requirements in article 5 – particularly MDR 5.5 a), b), c), f), g), and h) and equivalent IVDR requirements 5.5 a), b), d), g), h), and I) – which should be applied from the outset of and throughout device development, including any early preliminary studies.)

Question (e)

MDR Article 82 refers to provisions in Article 62 with the exception of 62.4(a)(e)(g)(i)(k). It is not clear why 62.4(e)(g)(i)(k) should be excepted. Also 62.4(a) will not be excepted if MHRA registration is required (as per question (d) above).

Question (f)

Research:

- If 'Research-use' is to be included in the HIE then it needs robustly and strictly defining, and clearly distinguishing from 'clinical investigation' and 'performance study'.

- The designation of devices as 'research-use' is susceptible to abuse as a means of users using devices inappropriately or manufacturers avoiding responsibilities; (as is recognised in the FDA's 2013 guidance on *In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only*).

- 'Research-use' devices are excluded from the IVDR but without definition. MEDDEV 2.14/2 gives guidance, (as does the FDA above, though that is a different regulatory scheme but offers some useful comparisons) – they must not be being put to any medical purpose and are generally either not really medical devices (i.e.: upon examination don't fall under the IVDR definition), or are IVD medical devices but at very early stage (i.e.: pre performance study) of development, (probably loosely analogous to the 'proof of concept' stage alluded to in the answer to question (d) above).

- If ‘research-use’ IVD devices are to be excluded under the HIE guidance then it would be highly desirable for the MHRA to offer an advisory service to which queries may be submitted for an opinion on whether a device application can be considered ‘research-use’ or not, (similar to, for example, the current MHRA service in advising on borderline products).

- There is no exclusion for ‘research-use’ devices in the MDR and the HIE should not introduce one – not least because there is no supporting guidance (e.g.: MEDEEV) to support such an exclusion, but also it is not clear why and in what circumstances it would needed / justified, and it will produce a ‘loophole’ that will inevitably be misused. If a device satisfies the MDR definition of a medical device then either full MDR or HIE apply.

- As a more general observation, the performance of a ‘research-use’ device has a direct bearing on the validity of the research results obtained and conclusions made. And whilst the research may not be directly affecting patient care at the time it is conducted, it may well influence future healthcare practices. As such, even if a research-use device is exempt from the IVDR (or its HIE), a level of rigour in its development and performance validation is still required.

The justification

QUESTION C
Please could you provide other examples that we can use to help health institutions understand what is needed?

Justification - Cost

The requirement in both Regulations is that ‘*the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market*.’

A common query is whether cost can be a justification for in-house manufacture? The HIE guidance needs to address this point – presumably this will need expert legal interpretation of the intent of the MDR/IVDR. Scenarios can include –

- a CE-marked device is available that meets needs at appropriate levels of performance, but the HI considers the device cost (or ongoing associated costs, such as consumables, servicing, etc.), to be to too expensive to be a viable solution;
- the desired device function is available at appropriate levels of performance, but only as part of a multi-functional (and hence expensive) CE-marked device - whereas the HI only needs that one of the many functions offered by the available multi-functional device.

It is worth noting that the real costs of in-house production of devices within HIs are often incompletely / poorly assessed; HIs should make full and realistic cost assessments if cost is to be a justification factor. If cost is relevant in justification, it should be the life-cycle cost of the proposed in-house manufactured device that is compared against the market competition, (i.e. cumulative costs of all life-cycle stages; including research and development costs, production, transport, use and maintenance, throughout the existence of the product to its disposal, clearance at end of service / utilisation).

Justification - Risk

The draft states “*the extent /detail of the justification should be proportionate to the risk class of the device*”. However, presuming the requirements for HIE justification in the

MDR/IVDR to be concerned with fair trade and not disadvantaging legitimate CE-marked device manufacturers, it is not clear to what extent 'risk' then influences the justification decision? Either a CE-marked device is available or not – irrespective of device risk?

Examples

If the guidance offers examples of 'justification' it should seek to select them judiciously, such as to represent the whole range of MD and IVD scenarios (Ie: hardware, software, reagents, genomics, etc.) It would be worth consulting different stakeholder groups for pertinent examples; (IPEM can provide examples relating to medical physics and clinical engineering activities).

Some clarity that the HIE does not need to be applied to CE-marked medical devices sold to market and intended to be adapted by a healthcare organisation e.g. wheelchairs with seating that needs to be adjusted, walking aids that need the height adjusting etc.

QUESTION D	
a) Should the health institution regularly monitor the market and test similar devices for equivalence?	No
b) Should the health institution stop making or modifying and using the device once an equivalent CE marked product is made available?	No
c) any other comments	

Question (a)
NO – For CE-marked devices, a HI will review the market when planning for equipment replacements; a similar approach for HIE devices would be reasonable, (see also answer (b) below).

Question (b)
NO – The HI will have gone to significant effort developing and producing the device and meeting the HIE requirements; it would not be reasonable for this effort to be discarded and production stopped simply because a CE-marked alternative has subsequently become available.
A product evaluation and risk / benefit assessment ought to be performed – only if the HIE device compares unfavourably with the new CE-marked device should production of the HIE device be ceased.

Question (c)
With regard to transitioning of legacy products -

- In-house manufactured devices already in use will not need recalling from service, any more than CE-marked devices commercially produced under the MDD/IVDD need recalling.

- For continued manufacture of pre-MDR/IVDR devices – commercial CE marking manufacturers are required to transition devices made under the old MDD/IVDD to the new MDR/IVDR; HIs should similarly transition pre-MDR/IVDR devices to the HIE requirements, if they intend to continue manufacturing them .

Information publicly available

QUESTION E

a) Should there be a register of health institutions applying this exemption?	Yes
b) Should parts A and B of the form be made publicly available centrally?	Yes
c) Should part C of the form also be made publicly available?	Yes
d) Should MHRA consider the need to carry out market surveillance activities of registered exemptions?	Yes
e) Any other comments	

Question (a)

YES - there must be a compulsory register – the HIE will be fundamentally ineffectual without one.

- MHRA oversight over activities under the HI exemption will not be possible if it does not know what activities are being undertaken.
- The requirement to register will provide a powerful message to HI management executives of their responsibilities / obligations - thereby ensuring that they are resourced and properly met. Without this public transparency activities in some HIs will not be to the required standards, (unfairly undermining those HIs that are diligent in meeting their responsibilities), and / or may even happen 'under the radar' altogether..
- It should be hosted by the Competent Authority (MHRA).
- It need only be simple, along the lines the MHRA's current on-line register of Class-1 devices under the Directive; a similar modest charging regime could apply
- It is consistent with the requirements for commercial manufacturers, who will all be registered under the new legislation
- The register information should include identification of the Class/es of the device/s registered.
- It provides a standard way for HI manufacturers to meet the HIE requirement, (MDR 5.5(e) / IVDR 5.5(f)), to make device information 'publicly available', (see question (b) below).
- Deadlines for registering could be the same as the transition periods for the Regulations, (3 years for MD, 5 years for IVD)?

Question (b)

YES - This can be the basis for making information 'publicly available' in a consistent and easily understood way, in a common repository; it effectively advertises HI in-house manufacturing activity to the public - thereby enabling them to identify activity and request the information that the Regulations require to be publicly available, should they wish to do so.

Question (c)

YES - Part C could be publicly available – though upon request from the HI rather than on central register (in the interest of keeping it simple to manage and use); the increased transparency achieved by making it available would improve HI diligence in properly meeting requirements.

Question (d)

YES – a risk-based MHRA approach to surveillance of HIE activities will be appropriate, and should be achievable, relying upon –

- compulsory register of HI manufacturers;
- requirement for reporting of all incidents involving in-house medical devices (i.e.: via the 'yellow card' scheme);
- an expectation of ongoing manufacturer vigilance / surveillance within HIs, as per MDR Article 5.5(h) / IVDR Article 5.5(i);
- the ability of the MHRA to request device documentation from the HI manufacturer should concerns arise, (Articles MDR 5.5(d) / IVDR5.5(e)), and the knowledge within HIs that the MHRA has this right.

It will be those HIs that do not register and make declarations which should be principal concern – hence the need for a robust requirement for HIE registration with the MHRA.

(e) Other Comments

- It may be beneficial in the early stages of introducing guidance and the MDR/IVDR coming into force that a number of HIs are visited and findings shared publically (possibly anonymously) to give feedback - including what is being done well as examples to how the HIE should be applied, and the way in which common challenges can be overcome.

Documentation requirements

QUESTION F	
a) Can these requirements be applied in emergency situations? – eg development of an assay for an emergent epidemic such as SARS or MERS?	Yes
b) If not what is the alternative route?	

Question (a)

YES - The health institution should already have the internal expertise, be on the central register, and have an established appropriate Quality Management System for in-house device development - so it should not be too onerous to achieve these documentation requirements. (If they do not have these then they are not an appropriate solution to meet the needs of the emergency).

In an emergency situation there might be some latitude for short-falls in non-critical aspects of documentation – with a view to rectifying these as soon as possible.

Question (b)

If the emergency really was such that unavoidably these requirements cannot be met, then it would be appropriate to require risk-assessed approval by the Competent Authority (ie: MHRA). Such circumstances would be very exceptional. Degree / scope of departure from requirements would need to agreed, and with a plan to retrospectively recover the shortfall as soon as possible afterwards, (to support reviews, lesson-learning, ongoing production, etc.).

QUESTION G	
a) Should this additional documentation requirement also apply to IVDs in class A, B or C?	Yes
b) If so, what is the robust, risk-based rationale and where can people go for guidance on IVD classification?	

Question (a)

There is no rationale for exempting Class A, B & C devices from this requirement –

- Technical documentation should not be viewed as an additional requirement - it is an essential element of product development, and so should be readily available.
- If this level of documentation is not available then product control is lax; exempting some products from this requirement sends the wrong message regarding expected standards of practice.
- Similarly, it would be contradictory and irrational to require this for all classes of MD, but not for all classes of IVD.

- This documentation should be a requirement for all devices (MDs and IVDs) - though it's depth will be proportionate to the device risk / classification, (as per EN 13485).

Surveillance

QUESTION H	
Should MHRA reserve the right to impose review and reporting requirements for all serious incidents plus trend reporting of other incidents in the future?	Yes
Yes, definitely. As above, this will push HIs to take the Regulations seriously. Surveillance practices are currently commonly weak for in-house devices (The requirement should cover - serious adverse events / incidents / public health threats.)	

Governance

QUESTION I	
Although not a requirement in the Regulations, should MHRA require health institutions to employ/subcontract/have access to competent regulatory advisers in lieu of a Person Responsible for Regulatory Compliance? (ref Article 15 IVDR and MDR)?	Yes
YES - definitely, there must be one of the above as an identifiable responsible person (RP). Ultimately somebody must take responsibility for meeting HIE regulatory requirements and signing the declaration. That would need to be one of the above, or somebody with access to one of the above. (If the Responsible Person relies upon expert advice from another to fulfil his/her duties, then the RP must confirm the advisor's competence to do so, and retain evidence of same.) Without such a person there will be inadequate control and poorly-defined responsibility / accountability. There will need to be some guidance on the expectations with regard to RPs – this could be a reference to Article 15 to provide guidance on the type of person and the duties and responsibilities of the role. For large organisations the range / scale of activities may be such that the role requirements could not be met by a single RP – either because of the volume of work involved and / or because of the different specialist expertise required in different sectors of HIE activity (eg: implants, sterile services, instrumentation, software, biomedical laboratories, etc.). Hence in practice the requirement might be met by a single RP for all of a HIs in-house device manufacturing activities - or there might be an RP for different sectors of activity. (This scenario is acknowledged in MDR/IVDR Article 15.4, requiring the areas of responsibility of each to be stipulated in writing). In the event that there are more than one RPs the guidance should recommend that there should be an organisational oversight framework / mechanism for coordinating and integrating their activities.	

QUESTION J	
a) Although not a requirement in the Regulations, should MHRA require or recommend health institutions to submit higher risk classification devices to a conformity assessment route using a Notified Body or other suitably qualified independent body?	Yes
b) If not should this be justified?	

Question (a)
YES - The levels of necessary expertise within HIs will be highly variable and often unscrutinised / unchallenged independently. NB involvement provides independent scrutiny and given their specialist expertise they actually add critical value (unlike, say a typical EN 9001 audit). NB involvement should be a recommendation, but not a stipulation. Recommend that NB involvement should be considered for higher-risk devices, especially implantable Class IIb and all Class III devices (including Custom-Made devices).

Question (b)
YES - If the HI's decision is not to involve a NB then that decision would be justified in the device's risk management file within the technical documentation – (under the auspices of a responsible person accountable for implementation of exemption requirements).

QUESTION K
How much cross over is there with FDA deliberations on Laboratory Developed Tests? http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/LaboratoryDevelopedTests/UCM536965.pdf
IPEM does not offer an opinion on this issue

Glossary

QUESTION M
Please list any additional terms that you would like to be included in a glossary.
• Collaboration what constitutes collaboration between organisations (as clearly distinct from 'transfer' of devices between organisations)
• Medical Device Accessory (ie: 'Accessory For Medical Device'. as per MDR Article 2.2) (ie: 'Accessory For An In Vitro Diagnostic Medical Device'. as per IVDR Article 2.4)
• Custom-Made Device (available elsewhere but would be useful to repeat here to avoid misconceptions)
• Manufacture
• Modification
• Refurbishing (versus Repair)
• Off-Label Use
• Research-Use Only (this definition is essential - see comments in response to Question B(f))

Page	Line	Comment	Text change	Rationale
all		Editorial (see Page 13 example below)	Review use of the word 'should' throughout this guidance document; where the guidance is based on a requirement in 5.5, then use the words 'must' or 'shall'.	Where the guidance is based on a requirement in 5.5, 'must' or 'shall' should be used.
all		Editorial	Use the abbreviation 'e.g.' rather than 'eg'.	
1		Add bullet points	• to be listed on a central MHRA register • .... • .... • ..... • a system for post-release ongoing clinical review	These should also be significant elements of the exemption requirements that need highlighting from the outset
1	42-43	That current guidance expires 2020 (MDR), 2022 (IVDR)	Add to the sentence: "… continues to apply until May 2020 (MDs) and May 2022 IVDs). After those dates the HIE must be applied as appropriate."	

Page	Line	Comment	Text change	Rationale
2	29-30	Change MHRA policy on not providing a PDF download for advisory documents such as this - (or at least make webpages convertible / printable to pdf without degradation)		This is already a difficulty with much existing MHRA information, which is now website only (and not printer-friendly so can't be converted to pdf either). There are many circumstances when a document needs to be circulated with papers for meeting such as for a Medical Devices Committee
4	2-4	Strictly speaking – – in-house manufactured devices were exempted in the IVD Directive, but – the issue was not addressed in the MD Directive. UK interpretation was that this meant in-house MDs were exempt from the Directive, but this interpretation was not universal across the EC.		
5	29	Suggest use of the term "medical device(s)" as the generic term throughout. The word "device" alone has an ordinary English meaning and is even more general. What word do we then use for a non-medical device?	Change- "device" to – "medical device" throughout	Use the term "medical device" as the generic term throughout, using MD and IVD abbreviation when differentiation is needed. (The word "device" alone is even more general – it could mean medical

Page	Line	Comment	Text change	Rationale
				device (MD or IVD) or non-medical device)
5	29	Add sentence to end of paragraph	Add text – "Accessories for medical devices are subject to the same requirements as medical devices."	
5	32-43	As per Line 29 above -	Change- "device" to – "medical device" in bullet-points	
5	37	This is an example of potential confusion in use of the word 'device' instead of 'medical device' (see previous note above"	Change – " ... using a product ..... not CE marked as a device" to – " ... using a device ..... not CE marked as a medical device"	A non-medical device could be CE-marked as a (non-medical) device - e.g.: an electronic instrument CE marked to the LV and EMC Directives – in which case this sentence then becomes confused
5	36	Edit the 5th bullet	Change to - • developing software that meets the definition of a medical device	Clarity

Page	Line	Comment	Text change	Rationale
6	8-9	Edit for clarity	Change to – "… use of sample types, accessories or components not specified by the manufacturer or combining devices in a manner not specified by the manufacturer. "…	
6	12-14	What if a modified device ostensibly retains original use and functionality, but renders the device less reliable, bypasses original safety features, makes the device more difficult to operate, etc.?	Text change along the lines of - from – "...function, performance or purpose has been altered." to – "...purpose, function, performance, operation or safety have been altered."	Inclusion of important less tangible factors in assessment of modification
6	23-24	Edit	… These devices will need to be CE marked by the manufacturer in the usual way.	
6 to 7	42 3	This is problematic, in that -. • HIs often provide maintenance/repair services within their own organisation, and to other legal entities (e.g. a large hospital providing services to a Community Trust);	Since the process of maintenance of medical devices (in the context of 'repair and maintenance') is not regulated by the MDR/IVDR, these Paragraphs need reconsideration, for the reasons outlined here (see left & right) .	At line 43, in what circumstances may such activity be 'placing devices on the market'? - given that the process of maintenance is not regulated. Which part of the MDR/IVDR would a HI providing maintenance services for medical electrical equipment to

Page	Line	Comment	Text change	Rationale
		• maintenance/repair services are not regulated under the MDR/IVDR; • nor is there justification in Article 5.5.of MDR/IVDR for applying the HIE to maintenance/repair services. Also there is danger of imposing requirements upon HIs that commercial organisations providing maintenance / repair services are not subject / working to. Consider 2 scenarios - – Manufacturer / authorised agent services own-brand devices to its own manufacturer instructions. – Commercial 3rd-party suppliers who provide 'multi-vendor' device maintenance / repair services; since they are commonly not authorised by the original manufacturer they do not have access to the manufacturer's technical manuals, support or training. In the 2nd scenario the service provider is not working to the manufacturer's instructions, but nor do they apply the MDR/IVDR.		another organisation need to apply? There is nothing relevant. The word 'repair' does not occur in the MDR. The word 'maintenance' in the context of 'repair and maintenance' occurs 10 times most often in Annex I, the GSPRs. In no case is the activity of maintenance covered by MDR requirements. The only wording that might be interpreted as 'repair or maintenance' is in the definition of 'reprocessing' in Article 2(39). *'reprocessing' means a process carried out on a used device in order to allow its safe reuse including cleaning, disinfection, sterilisation and related procedures, as well as testing and restoring the technical and functional safety of the used device;* However a further search on 'reprocessing' links this to single use devices on every occasion including in Recital 38. Is an anaesthetic workstation that

Page	Line	Comment	Text change	Rationale
				requires service and maintenance a ‘used device’? Even if it is, Article 17 does not apply since it is not a ‘single use’ device and Article 5.1 does not apply since its return to service from whoever and however it had been maintained is not ‘putting into service’ as defined at 2(29). There is no evidence to suggest, that the intentions of the Regulations were to bring service and maintenance of medical devices, other than those designated by the original manufacturer as ‘single use’, within its remit. The issue of ‘following manufacturers’ instructions’ in the context of maintenance is a separate issue (see ‘Comment’ left)
7	1-3		• Retain page 6 / lines 46-48, • But modify page 7 / line 1-3, along the lines of – from - “..... do not follow manufacturer’s instructions will need to apply the	Further to notes immediately above Consistent with the principles of Article 23.1

Page	Line	Comment	Text change	Rationale
			requirements of this exemption." to - ".. .. do not follow the manufacturer's instructions to an extent that this may constitute device modification as described above will need to apply the requirements of this exemption. Departures from manufacturer instructions must be assessed accordingly."	
7	8	Edit text	Change – " ... part or component ..." to - " ... part, component, or accessory ..."	There is an increasing problem with use of non-OEM accessories with medical devices – these sometimes of poorer quality / design that significantly affects the performance / reliability / safety of the device
7	13	Edit text	Change – " ... part or component ..." to - " ... part, component, or accessory ..."	There is an increasing problem with use of non-OEM accessories with medical devices – these sometimes of poorer quality / design that significantly affects the performance / reliability / safety of the device
7	10	Small edit	Edit to read: …shall be considered to be a modification of the device …	As worded, 'Items' not the process is the subject of the sentence.

Page	Line	Comment	Text change	Rationale
7	15	Edit for clarity	Change – "... no exemption is needed" to – "...the exemption requirements need not apply"	
7	after 16	Add text	Add a paragraph : "Health institutions who manufacture devices and/or accessory items that do not meet the MDR/IVDR definitions of medical device or 'accessory for a medical device' do not need to apply the requirements of this exemption. However, if such products are used in conjunction with medical devices the health Institution shall ensure through a risk assessment process that the item does not change the safety and performance or intended use of the medical device and supporting evidence to this effect shall be kept available."	
7	23	The issue of 'Research-use' only is very problematical and warrants some careful reconsideration – see comments in response to Question-		'Research Use' needs robustly defining, and distinguishing from 'clinical investigation' and 'performance evaluation'

Page	Line	Comment	Text change	Rationale
		B(f) above		
7	23	Non-medical devices can be CE marked (to other Directives / Regulations) – the intent of the text here is to specifically mean no CE mark to the MDR/IVDR, but the wording unintentionally excludes devices that might be CE marked but under other legislation	Change – " ... no CE mark" to – " ... no medical device CE mark"	Specify 'medical device' CE mark because products may carry a CE mark according to other Directives, (e.g.: machinery, low voltage. EMC, etc.).
7	30	As per 7/23		
7	33	As per 7/23		
7	37-39	Edit – - for a further scenario - for CE marking clarification	Suggest: - "Health institutions who procure or repurpose products labelled for 'research-use' or ~~otherwise~~ products without a medical device CE mark, and then use the product for patient management or in a manner that may influence patient care decisions will need to apply the requirements of the exemption."	Specify 'medical device' CE mark because products may carry a CE mark according to other Directives, (e.g.: machinery, low voltage. EMC, etc.).

Page	Line	Comment	Text change	Rationale
7	38	As per 7/23		
8	1	Change section title to –	"Performance studies (IVDR) and clinical investigations (MDR)"	Not everyone will be familiar with the subtle differences between the MDR and the IVDR, so suggest in the heading of this section:
8	2 to 4	Some further clarity of wording suggested	Devices made or modified and used in performance studies or clinical investigations are subject to the requirements of the Regulation, (particularly Chapter VI in both Regulations, which deal with clinical evidence, evaluation, investigations and studies), unless the requirements of the exemption apply.	Explicitly state the need for robust clinical / performance evaluations (including investigations / studies as necessary)
8	13-14	"... apply to the MHRA"	See comments provided above in response to Question-B above	More stipulation / clarification regarding notification to the MHRA under HIE (and comparison with requirements under MDR/IVDR)
8	after 16	Add text see comments in response to Question-B above	MDR 5.5 a), b), c), f), g), and h) and equivalent IVDR requirements 5.5 a), b), d), g), h), and i) will apply during development of exempted devices without commercial intent,.	

Page	Line	Comment	Text change	Rationale
			If a clinical investigation / performance study is carried out on a device in development under the exemption, the general principles in MDR Article 82.1 / IVDR Article 57 shall be applied.	The reference to MDR Article 82.1 / IVDR Article 57 may be insufficient – a broader reference to relevant Sections of Chapter VI MDR/IVDR should be considered
8	after 16	Add text see comments in response to Question-B above	Add / revise text in accordance with comments provided above in response to Question-B above	
8	45-47	" ... the health institution will need to decide for themselves ...." This will be unsatisfactory and is a source of confusion. The guidance should stipulate which requirements should apply to custom-made devices.	Add at end of 47 – "For devices that meet the MDR definition of a custom-made device, the requirements for custom-made devices, rather than the health institution exemption requirements, shall be applicable"	From the definition in MDR Article 2.3 (and the summary table on p9 of the draft guidance) it clear that it is the custom-made rather HIE requirements that are most appropriate for custom-devices, (not least the written prescription stipulation). This will also ensure a consistent approach for 'identical' types of custom-made devices, whether they be produced in-house or by an external supplier.
9	6-11	'Local validation' may commonly not be feasible, at least in any meaningful way – so likely to reduce to a paperwork exercise adding no real value (and hence potentially	Could the whole of the NHS be considered to be a single organisation for the purpose of sharing useful HIE devices, (provided that all sharing is for non-commercial actives – ie: not for	Enable sharing of HIE devices that are needed by the NHS but otherwise unavailable. Some hospitals will not have the

Page	Line	Comment	Text change	Rationale
		undermining credibility of HIE standards)	privatised health services – and that scale of transfers is non-industrial)?	capability to develop in-house devices, but as such are also unlikely to have the capability to meaningfully validate HIE devices provided by another HI. Hence implementation of the transfer requirement stipulated here may be susceptible to superficial implementation / abuse.
9	6	See question above regarding possible loophole for second-hand devices in our comments under 'Definition and Scope'.		
9	10-11	Meeting HIE exemption requirements for a device made and supplied by another HI will be problematical		In practice it is difficult to envisage how the receiving HI can satisfactorily / meaningfully meet the requirements of Article 5.5 for a device manufactured by another HI – particularly with respect to 5.5(f)(g)
10	9	Add to the examples	… or patient-transfer, mobility or support devices.	Although only examples, needs to include wheelchair and seating systems and the like.
10	33	Add an additional sentence	… available on the market. The requirement on the health institution is to 'justify in its documentation': there is	

Page	Line	Comment	Text change	Rationale
			no requirement to seek prior approval from the Competent Authority.	
10	34	Comment on "… market surveys …"		If cost is to be an acceptable justification then the market could be tested for CE-marked equivalents, against a proposed HIE device, by competitive procurement exercise of the type routinely used when selecting from competing commercially available CE-marked offerings.
11	3	Edit text	Remove wording – "…~~(including invasive sample taking)~~	This is an unnecessary specification – if it is to be included then there are many other scenarios which could warrant inclusion too
11	4	Add text	Add after first bullet-point: ● device functionality	Functionality is what the device does, performance is how well it performs these functions (i.e.: to what specification)
11	4	Add text	Add after third bullet-point: ● device safety	

Page	Line	Comment	Text change	Rationale
11	5-6	Remove text	Remove wording – ● ~~device requirements~~ ● ~~turn-around times~~	• Not clear what is intended 'device requirements' (and 'requirements are captured in the other bullet-points anyway – i.e.: needs, function, performance, etc.) • Turnaround time of what? diagnostic test results?
11	9	See notes in repose to Question C above, querying whether cost can be an acceptable justification criteria?.	Add to the end of the bulleted list: ● cost effectiveness	Prohibitive cost, rendering 'practical unavailability', can be considered a critical factor in itself. If cost is to be an acceptable in justification, then it should be whole life-cycle costs that are compared (not simply the device purchase cost) – i.e.: including consumables, maintenance / reprocessing, etc., etc..
11	10-11	See comments regarding 'risk' in response above to Question C		
11	31	That a distinction is being made between QMS for manufacture and QMS for usage needs to be made very clear	Insert text – "…. exemption is that both manufacture and use …."	

Page	Line	Comment	Text change	Rationale
11	32	Formatting edit, to avoid any confusion between quality systems for manufacture and quality systems for use.	Insert paragraph break – " …. quality management systems. EN ISO 13485 is an …."	After this adjustment – 1st paragraph ("One of ….") refers to both manufacture and use, 2nd paragraph ("EN ISO 13485 ….") refers or manufacture only 3rd paragraph ("For advice on ….") refers to usage only
11	32-40	That a distinction is being made between QMS for manufacture and QMS for usage needs to be made very clear	Restructure wording in first sentence of para 2, so that it begins – "For manufacture of medical devices, EN ISO 13485 is an appropriate …." restructure wording in first sentence of para 3, so that it begins – "For use of medical devices, advice on appropriate ……."	
11	38-40	Remove / correct this reference	Remove or correct the reference to this document (see notes to right)	Actually that MHRA guidance document does not say much on QMS per se (and nothing on QMS for 'use') – and its emphasis is more concerned with device management than device usage. Also, if this reference is retained then - • correct the date of latest version to April 2015

Page	Line	Comment	Text change	Rationale
				• also give reference to the corresponding MHRA guidance document for management of IVDs (*Management of In Vitro Diagnostic Medical Devices* – December 2013)
11	40	Be more specific.	Add after: …April 2015. Robust systems of local clinical governance, subject to the CQC inspection regime, (or home nation equivalent), may be considered to constitute quality management systems for the use of medical devices under the exemption	The link to Managing Medical Device 2015 in section 2.6 is a bit tenuous. Most users of medical devices won't have 'QMS' as such, but will have systems of clinical governance, etc.
11	47	Meaning unclear; why is the last part of the sentence necessary; what does 'harmonised to' mean?	Delete – "… ~~and harmonised to the IVDR/ MDR~~."	
12	2-6	In the IVDR - 5.5(b) says manufacture & use of devices must be under an appropriate quality system 5.5(d) says laboratory must be compliant with EN 15189 These are listed as separate	Reconsider this section, since – EN 15189 is not an adequate standard for production of many types of IVD medical device products (eg; IVD apparatus / instruments, software, etc.) – nor could UKAS audit such products	Challenges regarding use of EN 15189 as the medical device QMS for HIE include - • EN 15189 deals with laboratory activities, whilst it might be adequate for lab manufacture of IVD types such as reagent kits, etc.– it is not applicable /relevant

Page	Line	Comment	Text change	Rationale
		requirements – EN 15189 is not necessarily specified as being the means for meeting (b) –see notes in Rationale column to right	EN 15189 might be usable for lab-produced IVDs such as reagents / assay kits / etc. (which is the more common type of IVD activity in HIs) - though if used in this context the HI should need to confirm that the QMS expectations outlined in IVDR Article 10.8 are adequately addressed.	to manufacture of IVD devices such as hardware/apparatus or software; • the difference is further reflected by the fact that EN 15189 is audited by UKAS, which do not have the competencies now required of medical device Notified Bodies; UKAS have the capability to audit laboratory-type activities but not other types of medical devices manufacture • EN 13485 has tables correlating itself to the requirements under the MD and IVD Directives (and CEN/ TR 17223 does the same for the new MDR/IVDR); there are no such correlating tables in EN 15189.
12	14	Change text	Change – " … to make some information publicly available" to – " … to make <u>a declaration together with</u> some supporting information publicly available"	See also Note p15 / line 11

Page	Line	Comment	Text change	Rationale
12	after 17	There needs to be a public register (see comments above in response to Question E)	Add two paragraphs along the lines of … Health Institutions may be required by the MHRA to provide information on their exempt medical devices upon request. The MHRA shall be permitted access to inspect exempted activities within Health Institutions. In order to facilitate competent authority oversight, and to provide for the making public of declarations, the MHRA requires health institutions undertaking in-house manufacturing of medical devices to register these activities with the MHRA, who will make the register available on the MHRA website. The Form for MHRA registration is provided in Annex ??.	From Article 5.5 Register enables MHRA oversight and the making public of information The register only needs to be as simple as the current Class I manufacturer register maintained by the MHRA, but must indicate the device type and the risk Class that the device falls into. All activities are thus publicised, enabling identification of activities by both the MHRA and the public. Declarations can then be provided by HIs upon request.

Page	Line	Comment	Text change	Rationale
12	39	Correct text	Correct text from “performance evaluation” to – “performance study”	
13	9-12	Consider text removal	Change – “Annex Z of a …… to IVDR and MDR” to – “Annex Z of a harmonised standard maps the clauses of the standard to the corresponding requirement of the legislation.”	The discussion with regard to Directives may be more confusing rather than illustrative, now that we are transitioning to Regulations
13	12-13			Urgent work has started in the European Standards organizations CEN and CENELEC to develop, in the same format, appropriate Annex Zs for the IVDR and the MDR. They have been mandated by the Commission to get on with this,. 13485 and 14971 being the top priority.
13	15	“may wish to ...” is too weak	Change – “may wish to use” to – “should consider use of”	Even manufacturers of CE-marked devices are not obligated to use harmonised standards, but in practice there is an implicit expectation that relevant standards are at least

Page	Line	Comment	Text change	Rationale
				considered before a decision not to use them, (and good product technical documentation ought to include explanation of that decision) – similar rationale ought to apply to HIE
13	22	Edit text	Change “IVDD” to “IVD”	See comment above
13	26	Edit text	Change “MDD” to “MD”	See comment above
13	34-35	See comments above in answer to Question G, regarding documentation for Class A,B,C IVDs	Change “class D IVDs” to “IVDs”	
13	35 and 44	As per suggestion above to review the Use of ‘should’ throughout this guidance document. Where the guidance is based on a requirement in 5.5, ‘must’ or ‘shall’ should be used. For example …	Change wording at line 35 ... To apply the exemption, the health institution ~~should~~ must prepare documentation that describes: … At line 44 … The documentation ~~should~~ must be sufficiently …	
14	25	*must* not *should*	During manufacturing or modification of the device, the health institution ~~should~~ must make sure …	

Page	Line	Comment	Text change	Rationale
14	30	*must* not *should*	… institution ~~should~~ must have a surveillance system in place …	In line with the **requirement** in 5.5 (h)
15	11	" … included in the declaration" What declaration? – this has not been raised / explained prior in the document (other than in one cell of the table on p9)	Add a prior sentence specifying the requirement for a public declaration, and /or make the change suggested Page 12 / Line 14	
15	16	Edit text	Change "declaration" to "declaration(s)"	Large / complex HIs may have a number of different medical device production activities – for which it may be more appropriate to have separate declarations for different activity groups
15	18	Typo with reference to the MDR	… (See Article ~~16~~ 15 for guidance on responsibilities) …	
15	20	Suggested addition	Add an expectation that HIs establish and maintain a single internal list of all medical device manufacturing activities being undertaken within their organisation	This would be very helpful (essential) for those responsible for governance management within the HIs

Page	Line	Comment	Text change	Rationale
15	22	See Comment above regarding responsible person, in response to Question I		We consider that Responsible Person/s (employed or access to) must be a requirement
15	after 35	Involvement of Notified Bodies	Insert text along the lines of … Health institutions should consider formal external assessment of exempt devices by Notified Body and /or other independent body, particularly for higher risk MDs and IVDs, A decision not to do so should be justified in the risk management file and recorded within the technical documentation.	This allows flexibility but puts onus on decision makers to risk justify decisions not to involve NBs, not merely to avoid cost/difficulty.
16	8		Change – "Devices that are made under ...." to – "Devices that are manufactured or modified under ...."	

Page	Line	Comment	Text change	Rationale
16	10	Change text - Legacy (MDD/IVDD) in-house manufactured/modified devices already in use can stay in use, but continued production of more of them requires transition to HIE.	Delete – ".. ~~or until a significant change in the device~~" add new sentence – "Continued production of such devices beyond the transition deadlines will require the HIE to be applied. "	- If legacy products do not transition to HIE then there will be an anomalous situation whereby legacy devices are being produced without being on the central MHRA register, without publicly available declaration with related information, etc.. (Thus continued production older pre-HIE devices, of potentially poorer quality, would be uncontrolled – in contrast to controls on newer HIE products) - This transition should not too onerous for well-made products
17	4-5	Additional text	Will submission of Forms A and B be the basis for submission to a central MHRA register? – in which casee add text to explain as much	A compulsory MHRA register of HIs under the HIE is definitely needed (see comments in response to Question E)

Page	Line	Comment	Text change	Rationale
17	6	Remove text?	Remove Line 6?	Is Form C necessary? This information should be an essential part of technical documentation which the HI compiles for the device – so the HI could just provide the necessary extracts from the technical documentation upon MHRA request?
19	3 table row 2	Add text	Change - “Name” to – “Name of Health Institution”	For clarity
19	3 table row4	Add text	Change - “Name of contact” to – “Name of Responsible Person”	Or some similar title, in accordance with the finalised requirements in this guidance, that reflects this is the person with designated accountability / responsibility
19	3 table row 5	Edit text	Change - “Department” to – “Department(s)”	There may be more than one responsible person- see Comment above regarding responsible person/s, in response to Question I.

Page	Line	Comment	Text change	Rationale
20		Modify table	Modify table to allow HI to list which departments are producing which devices	Large / complex HIs may have many disparate medical device actives being undertaken in different parts of the organisation see Comment above regarding responsible person/s, in response to Question I.
22	5-6	GSPR checklist	Remove GSPR checklist Could replace, for example, with a simple free text box titled along the lines of - “Statement of compliance with the General Safety & Performance Requirements of the MD/IVD Regulations (detailed to be provided of any requirements not fully met, with due justification)”	GSPR compliance assessment cannot be summarised this simply – applicability / compliance needs to be against each sub-clause, (eg: some elements of, say, “Chemical, physical & biological properties” may apply and some may not, etc., etc.) Full GSPR compliance analysis should be an essential part of the techno documentation, which could be made available on request.

Use new pages as required