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Position paper

18 October 2019

AnimalhealthEurope comments to the EMA advice to the European Commission on the Union Product Database

Implementing measures under Article 55(3) of Regulation (EU) 2019/6 as regards the Union product database and the technical and functional analysis necessary for its establishment

General comments

AnimalhealthEurope is supportive of the legal basis given to the creation of a Union product database (UPD) and welcomes the opportunity to comment on the EMA advice (EMA/392996/2019).

The development of the UPD is a highly complex and challenging project specifically in view of the implementation deadline and the interdependencies with other systems in the EU telematics landscape. In this context the possibility to provide comments as early as possible in the process is highly appreciated.

The EMA advice is a much welcome step towards a transparent development and a common understanding of the functionalities of the future system.

In view of the existing resource constraints it is applauded that the approach advises that the UPD should be built

- Utilising existing functionalities and experience from ongoing developments in the network, as far as possible.
- In a step-wise manner focussing on key legal and business requirements first but keeping the overall vision for further development in mind.

It is also welcomed that the EMA advice lays out a comprehensive picture of what needs to be developed, although this means the complete advice does also contain more information than to be included in a legal document. As indicated in the advice only 'Must' requirements should be considered in the implementing act for delivery of the UPD by the date of applicability of the Regulation. The 'Should' requirements are also important if the full benefits of the UPD are to be realised and these should also be mentioned in an implementing act with a realistic target delivery date after January 2022.

On the other hand, further technical specifications like the detailed conceptual data model are valuable to direct the UPD development but are likely to be subject to change during the development process and therefore should not be included in the implementing act.

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Major comments

AnimalhealthEurope very much:

- Welcomes that it should be possible to introduce in the UPD different modalities of changes in parallel (cf. p.3 of the EMA advice);
- Welcomes the statement that not all variations without assessment have to be transposed into a data field in the UPD (cf. p.29);
- Supports maintaining the possibility to group changes, that is to say, link in a single database entry e.g. the same change to different products or different changes to one product;
- **Recommends** that the future implementing act should detail a process or mechanism for Marketing Authorisation Holders (MAHs) to request correction to product data in the UPD in case of data quality issues;
- **Seeks clarification** whether the present advice is compatible with the implementation at UPD roll out of the vision from the ROG for simplification of regulatory procedures. Simple changes such as the name change of a legal entity could be done through database updates (OMS first, then UPD, both being interfaced) without needing the submission of a variation, in the current meaning of the term;
- **Reiterates our strong concern** on the development status of the UPD. AnimalhealthEurope has recently written to DG Santé expressing grave concern and the need for UPD to be delivered on time and would like to make a strong plea that appropriate financial and human resources are made available to achieve these objectives.

Functionality for group variations:

The UPD must allow a single variation not requiring assessment to an unlimited number of different marketing authorisations, including allowing a single dossier upload to support the variation, for example through a compatible CESP module for veterinary medicinal products.

This means that it must be possible to group such changes so that there is a 1:n relationship between the field "Variation classification" and the variation procedure to allow grouping of several variation classification codes.

GTIN:

AnimalhealthEurope recommends that GTIN is added under section 2.3.2 as a structured data element. This would allow it to be used as a harmonised identification code which may be used to replace the marketing authorisation number (Article 11 NVR), so facilitating aggregation and/or granularisation of data for pharmacovigilance purposes, electronic leaflets and improved traceability.

Access to legacy data:

A testing environment for the bulk upload of legacy data must be available 6 months before the implementation deadline in order that the UPD contains accurate and complete data at implementation.

To achieve this, it would be helpful if the Implementing Act set milestones, progress reporting requirements with timelines that allow sufficient time for upload of legacy data by the Agency and national competent authorities (NCAs) and for testing by NCAs and industry.

Product data for pharmacovigilance:

It is essential that provision of product data, including sales volumes for pharmacovigilance, is available at implementation of the database to avoid multiple data entry.

Regulation 2019/6 does not request sales data down to the packaging level (c.f. page 8 of the EMA advice). The granularity of the sales data should be sufficient for pharmacovigilance purposes and should not go beyond. AnimalhealthEurope requests that the development of detailed guidance and requirements for provision of sales data receives an early priority and is also a collaborative approach involving the Agency, NCAs and relevant stakeholders including MAHs (*please refer to the position paper on sales data provided in the AnimalhealthEurope Supplementary Package of position papers on the implementing measures, August 2019*).

Interoperability of databases:

AnimalhealthEurope very much supports the interoperability and interfaces between the different databases in order to realise the potential benefits of the UPD and minimise data entry. The principle of entering a piece of data via one portal into a database which has appropriate interfaces to allow sharing of the (identical and unchanged) data with all of the other databases / systems that need to use that piece of data, is essential for the UPD to achieve the expected objectives and efficiencies. We make further reference to this in the specific comments section below.

Interaction with Industry:

Industry will be a key user of the UPD and it is essential that it is able to interact and input into the database development at the appropriate level in a practical and timely way to ensure that the delivered system is fit for purpose and achieves its objectives. This means that additional opportunities for interaction other than at the strategic level of TMB must be established.

The implementing measure's advice mandate, which stresses the 'utmost importance of governance that helps to respect deadlines, deliverables and the financial planning', can be achieved in full transparency through inclusion of milestones, progress reporting and defined timelines in the Implementing Act and would facilitate practical interaction with all stakeholders including industry, to the benefit of all.

Specific comments or detailed analysis:

Page Number	Comment
Page 4	Business process diagram: We understand that the subprocess "Update product data" is a technical step only without specific interaction with NCA or industry users. Updates can be applied automatically either based on submission by industry / NCAs or after approval by NCAs for those changes not requiring scientific assessment. Please note that after rejection of a change the sub-process "update product data" should be skipped.
Page 5, BR-01-002	If the creation of new product entries by competent authorities at the end of the assessment phase for MRP/DCP products is needed to support variation procedures, then the requirement should be upgraded to 'Must'.

Page 6, BR-01-009	Support of consistent common data of product entries following SPC harmonization should be considered as well.
Page 6, BR-01-011	Ensuring data consistency is a must. Instead of establishing complex data exchange mechanisms for that purpose, the feasibility of reduction of the number of NCA systems should also be evaluated.
Page 6, BR-01-013	After a change notification, the MAH should ensure alignment of their own database. At the current stage the need for an API to automatically transfer data to the MAH system is not high. Thus, to ensure focus on more important topics the classification should be changed to "Could".
Page 6, BR-01-014	There seems to be incoherence between BR-01-008 ("Must" requirement) and the "could" here as the link between OMS and EUDRA GMDP would allow to extract manufacturing sites data automatically.
Page 7, BR-01-015	Interoperability of databases: effective interface with EV Vet 3 is needed. Provision of product related data including sales volumes appears to be a "Must" for pharmacovigilance purposes instead of a "Should" in order to avoid entry of the same information in several databases. On the intended level of data aggregation e.g. while data is required on pharmaceutical form level, the assumption is that this does not exclude other (lower) levels of aggregation like strength.
Page 7, BR-01-018	Is this "should" classification related to the timing only? Otherwise the possibility appears to be a "Must" to ensure timely population of the UPD.
Page 7, Section BP-1 and Page 9 Section BP-2	In order to ensure sufficient transparency, the UPD should allow identification of periods of protection assigned to the technical documentation on which the marketing authorisation is based. It is therefore recommended to add the following requirements, classified as "Should" Section BP1 "BR-01-019 The system shall allow identification of the end of any period of protection of technical documentation after the first marketing authorisation." Section BP2 "BR-02-015 The system shall allow identification of the end of any prolonged or new period of protection of technical documentation after post-authorisation changes to the marketing authorisation."
Page 7, BR-02-002	This requirement should be classified as "Must". If this requirement is not in place for initial implementation, this might mean that the record of the change provided to concerned authorities will not include information on the current master data that is changed. This could be an obstacle to a swift process for the confirmation of the change in the UPD. This is supported by the classification as "Must" of requirement BR-03-002.
Page 8, BR-02-005	This requirement should be classified at least as "Should" to align with BR-02-004 classification and with what it is stated on page 19 that "some sort of data versioning must exist in the UPD". If the option to obtain report on the history of the changes to the dataset in the UPD is available for authorities, this should as well be granted to MAHs according to their specific access rights.

Page 8, BR-02-007	In this document it is proposed that "MAH must be able to submit annual sales data **at package level** for authorised products on the market to fulfil their legal obligations." This sentence should be amended as the requirement in the Regulation 2019/6 is to the MAH to submit annual sales data for each of its VMPs only. Signal management may require sales information for these VMPs down to the level of marketing authorisations but there is no need for a default request for sales data at package level. The granularity of the sales data should be sufficient for pharmacovigilance purposes and should not go beyond.
Page 9 Section BP-2	A key requirement for the handling of variations is to allow bulk changes affecting several marketing authorisations. It is therefore recommended to add the following requirement classified as "MUST": "BR-02-016 The system allows to relate a single variation requiring no assessment to an unlimited number of different marketing authorisations"
page 9, BR-03-005	The possibility to give access to other user to manage product data on their behalf appears identified as a "should" has to be changed into a "must" in the first version of the UPD. As 'Should' this may not be available at deadline. In this case SMEs that use consultants may not be able to manage product data & so fulfil their responsibilities.
Page 15, table	Approve *or reject* variation without assessment.
Page 27, Section 2.3.2	Changed descriptions or other additional data fields may need to be added here as identified in below comments on the Conceptual Data Model.
Page 27, Withdrawal period	Format of withdrawal period should be free text "*when structured data is not possible*"
Page 27 Section 2.3.2	A data field should be included to cover the legal option of a harmonised identification code (e.g. GTIN) which according to Article 11 of the Regulation may be used to replace the marketing authorisation number (see also comments regarding the use of GTIN in the comment section on the Conceptual Data Model below)
Page 29, 2.4. Interoperability and interface	AnimalhealthEurope supports these principles (largely in line with the position paper on interoperability of databases), especially with regard to single source for each type of information (also p34). It supports the statement that the 'UPD should consume data from other existing databases or IT tools to avoid duplication of data' but would have expected the scientific advice to list those databases or IT tools that either exist or are under development: the R, O and S components of SPOR; the P component of SPOR, pending the decision if PMS is the basis of the UPD; CESP; EUDRA-GMDP. The vision for the long-term could have also expanded on the benefit of interfaces with regulatory procedural systems such as CTS.
Page 31	"the UPD is not envisaged as being used for live support to e-prescription systems" It is agreed that the UPD is not currently envisaged as a support to e-prescription systems (although the UPD would be the most obvious support should such systems be ever contemplated for the veterinary sector. However, electronic product information (ePI) in the veterinary sector would improve the quality of information flow to veterinarians and animal keepers, in particular by increasing the speed that (important safety) changes became visible to the end users, assisting the MA Holder comply with its responsibilities under the Article 58.4 (The

	marketing authorisation holder shall ensure that the summary of product characteristics, package leaflet and labelling is kept up to date…). Regulation 2019/6 allows (Art 12.3) for a National decision on how pack leaflet is made available: paper, electronic or both. The UPD should be set up in a way that does not hamper a future change from PDF-based PI to ePI.
Page 37, Annex III, EU TMB	While the option to provide input on a strategic level at TMB meetings is appreciated, the frequency of interaction with industry as future key user of the UPD has to be higher and also on a more practical level to ensure that the delivered system is fit for purpose.
Page 41, Annex IV	Parallel distribution – Products subject to parallel distribution are not specifically mentioned in the document.

Comments to the Conceptual Data Model (CDM)

Page 23 (CDM)	Relationship between Regulatory Entitlement and Medicinal Product/ Packaged Medicinal Product: - The XOR relationship for Medicinal Product / Packaged Medicinal Product appears to be difficult to develop from a technical perspective. Proposal is to cut the relationship between Regulatory Entitlement and Packaged Medicinal Product and to maintain regulatory data which need to be broken down to the package size level (like authorisation number) optionally on the level of the package size. - The Regulatory entitlement has a n:n relationship to the Medicinal Product. Should this be a 1:n relationship? Noting that the source product for parallel trade is displayed separately, it is unclear how a medicinal product (NB not a "pharmaceutical" product) can be related to more than one entitlement in a specific country. E.g. even duplicate applications would relate to different medicinal product entities with different product names.
Page 23 (CDM)	Regulatory Entitlement: Authorisation number may be package-size specific
Page 23 (CDM)	Medicinal product / Packaged Medicinal Product: Entering "legal status of supply" on both levels bears the risk of data inconsistencies.
Page 23 (CDM)	Medicinal product: - There may be more than a single route of administration (1:n relationship) - There may be more than a single legal basis (e.g. MUMS and Article 12(3) application)
Page 23 (CDM)	Medicinal product: Category of product (e.g. authorised VMP, homeopathic product etc.) appears to be a duplication of the information under Regulatory Entitlement.
Page 23 (CDM)	Medicinal product: To be confirmed whether more than a single ATCvet code might be allocated to a product (e.g. for vaccines?). A 1:n relationship might also allow future flexible entry of other product code types.
Page 23 (CDM)	Medicinal product:

	What is the difference between the permanent identification number and product identification number? (in med product yellow box). Could these be the same? To be clarified. See also p27
Page 23 (CDM)	Medicinal product name Unclear why this is classified by "country" and not by "language". The assumption is that the data is needed for countries with more than one official language or English translations of the official name.
Page 23 (CDM)	Variations not requiring assessment Responsible Country – Proposal to replace by "Responsible Authority" as referenced via Organisation (note that there may be more than one NCA per country). Variation classification: There should be a 1:n relationship between this data field and the variation procedure to allow grouping of several variation classification codes.
Page 23 (CDM)	Organisations: The product owner (e.g. MAH) organisation appears to be missing.
Page 23 (CDM)	Document: To accommodate changes through variations a status should be assigned to the document (e.g. current, version).
Page 23 (CDM)	Market information Unclear why this has a n:1 relationship to Medicinal product. In addition, this data appears to be a duplication of information available on package size level, i.e. it could be generated also by aggregating the marketing information of related package sizes.
Page 23 (CDM)	Withdrawal period The withdrawal period needs to be related to target species, administration route and tissue.
Page 23 (CDM)	Substance It is assumed that this relates to active substances only. See also page 26 (data field "active substance").
Page 23 (CDM)	Target species Unclear why there is a n:n relationship to Medicinal product instead of a n:1 relationship.
Page 23 (CDM)	Packaged Medicinal Product: It is strongly recommended to allow inclusion of a harmonised identification code (GTIN) at this level. This would enable numerous future use cases like aggregation of data for pharmacovigilance purposes, electronic leaflets or improved traceability (NB: not 'serialisation', which is not necessary or appropriate for the VMP sector).
Page 23 (CDM)	Marketing Status - As this section addresses both start of marketing and stop of marketing the "marketing date" should read just "date" to allow flexible date entry depending on the context. - Unclear why marketing status is both related to the medicinal product and the packaging size, again this may lead to inconsistent data entries.

Page 23 (CDM)	Sales Information - The section should identify the reporting date / period down to month / year to allow more flexible reporting times. (Note that also on page 29 an "(at least) annual" reporting frequency is mentioned.) - Clarification should be provided how global signal management (i.e. including 3rd country reporting) can be performed. It is recommended to include at this level o identifiers independent of EU authorisations to identify packages (i.e. GTIN) o identifiers for pharmaceutically same/similar products (e.g. PhPIDs) o Local brand names for human-readable identification of non- EU products
Page 23 (CDM)	Incidence calculation Data to allow incidence calculation is currently missing in the data model. The following information should be considered related to the sales volumes via a unique identifier like GTIN - Species. - Country (for multi country articles). - Number of treated animals. - Optionally parameters used for calculation of the number of treated animals like species split may be included.
Page 23 (CDM)	Packaged Medicinal Product / Strength: Please clarify why this is a 1:n relationship. Normally one product strength would relate to one or package sizes but not vice versa.