

DRAFT FOR PUBLIC CONSULTATION

HMA/EMA GUIDANCE DOCUMENT ON THE IDENTIFICATION OF COMMERCIALY CONFIDENTIAL INFORMATION AND PROTECTION OF PERSONAL DATA WITHIN THE STRUCTURE OF THE MARKETING AUTHORISATION (MA) DOSSIER - RELEASE OF INFORMATION AFTER GRANTING OF A MARKETING AUTHORISATION

The Heads of Medicines Agencies (HMA) and European Medicines Agency (EMA) have been working together with a view towards achieving greater transparency of their operations and better addressing the increasing requests for information they hold from members of the civil society.

This draft guidance document is presented as a consensus document agreed by the entire Network of Competent Authorities, laying down practical orientations for national and European authorities in regard to requests for access to information contained in MA dossiers. Notwithstanding this guidance document, it should be noted that National Competent Authorities and EMA ultimately are required to follow national or European legislation in terms of access to documents.

HMA have agreed in their meeting in Visegrad 28 April 2011 to start a public consultation on this document to hear the view of concerned stakeholders (including pharmaceutical industry, healthcare professionals and patient organizations) before a final version of the guidance document will be agreed upon.

Applicability to Veterinary medicines

At the present time the way in which these principles should be applied in practice has only been considered in detail for human medicines where the CTD is the standard format for submission. Work has started between the EMA and CMDv to consider practical implementation in the veterinary field and it is anticipated that a more specific consultation will be organised with veterinary stakeholders towards the end of 2011. Nonetheless, in view of the fact that no distinction is made in legislation as to the principles that apply when dealing with access requests between the human and veterinary sectors, the same principles are expected to be applied. Feedback is therefore invited from stakeholders involved with both human and veterinary medicines.

Requests for specific and detailed feedback

Stakeholders are particularly invited to comment on the following topics :

- Release of Personal Data (e.g. CV, signatures etc);
- Contractual arrangements between different companies;
- Personal security of individuals involved in any way with studies involving animals (bearing in mind that such studies are only permitted where non-animal alternatives are not possible)

Facilitating responses to access to document requests – invitation for industry proposals

Both EMA and National Competent Authorities receive an increasing number of requests for access to documents. These requests require a considerable amount of resources to check and redact the documents in order to identify commercial confidential information and personal data that may have to be protected.

Marketing Authorisation Holders are therefore invited to submit proposals on how within the CTD structure a dossier can be created where the commercial confidential information (CCI) and protection of personal data (PPD) can be concentrated in a single section. Such a system is already in place in other sectors and would save resources within the agencies when dossiers should be released without disclosing CCI and PPD.

Deadline for comments: 1st September 2011

Comments should be sent before September 1st 2011 to the following mailbox:

HMA-EMATransparencyConsultation@ema.europa.eu

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According to the HMA/EMA recommendations on transparency approved in November 2010 - Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation (EMA/484118/2010):

- A common approach should apply for active publication and for disclosure upon request for access to documents. Such approach would be useful with regard to information considered as commercially confidential during the evaluation process of applications for marketing authorisations and when the opinion/decision is taken.
- EMA and National Competent Authorities should have a common approach on what should be considered as commercially confidential, in particular whilst procedures to assess marketing authorisation applications are ongoing. In view of the lack of a legal definition and for the purpose of harmonisation 'commercial confidential information' shall mean any information which is not in the public domain or publicly available and where disclosure may undermine the economic interest or competitive position of the owner of the information.

HMA and EMA have agreed on the following recommendations to facilitate a common and consistent approach across the European Union to provide guidance on the identification of commercially confidential information or on personal data provided in the MA dossier after a Marketing Authorisation is granted, when dealing with request of access to documents at EU level.

This guidance document is intended to be applicable to information on medicinal products assessed under the national, mutual recognition, decentralised and centralised procedures, according to the relevant legal and policy references on publication or access to documents [e.g. the EMA policy on Access to document or the HMA/EMEA recommendations on Transparency - Recommendations on the handling of requests for access to Periodic Safety Update Reports (PSURs)].

The Assessment Reports summarise the data in the MA dossier, which is the primary source of information, and present the discussions and conclusions of the scientific committee(s). The same principles for redaction of commercially confidential data and protection of personal data may therefore apply when disclosing the Assessment Reports.

This guidance addresses the approach to provide access to different information in the MA dossier as high-level principles. This guidance document follows the structure of the Common Technical Document (CTD). However the principles outlined should be equally

applicable to other formats and applications (e.g. Orphan designation, Paediatric Investigation Plans).

This guidance document is intended to be a consensus document agreed by the whole Network, which could lay down practical orientations for national and European authorities in regard to the release of the MA dossier upon request. Notwithstanding, this guidance document it should be noted that National Competent Authorities/EMA have to follow their national legislation in terms of access to documents.

Guidance is therefore proposed according to the following format:

1. All sections of the structure of the MA dossier have been classified according to 4 criteria:

CCI (Commercially Confidential Information¹): means that the section contains commercially confidential information **and therefore cannot be released (the corresponding section of the CTD has to be redacted)**

PPD (Protection of Personal Data): means that the section may contain personal data that have to be protected and **therefore cannot be released or should be redacted before release.**

CBC (Case-by-Case analysis): means that the section may have commercially confidential information or personal data, thus suggesting a case-by-case review prior to its eventual release.

Can be released: means that all of the section can be released.

2. Additional Principles to be applied for the Redaction of Commercially Confidential Information.

These recommendations apply to the granting of access to the MA dossier after approval, refusal or withdrawal of a marketing authorisation application and to the disclosure of assessment reports,. They should be read in conjunction with the above classification of the different part of the CTD and aims to facilitate redaction of the sections classified as CCI.

Information that is already in the public domain is not considered as commercially confidential. Nevertheless, when information has been in the public domain through a breach of the law, it could still be considered confidential in accordance with the principles of this document. However, the owner of the information has to inform the respective National Competent Authority/EMA in writing on the breach of law.

2.1 Information on the Quality and Manufacturing of Medicines

A general principle regarding quality and manufacturing information is that detailed information is commercially confidential but general information should be disclosed.

2.1.1 Composition and product development

In general, pharmaceutical development information is commercially confidential. This includes detailed data concerning active substance, formulation and manufacturing and test procedures and validation (see later).

¹ For the purpose of this guidance document, 'commercial confidential information' shall mean any information which is not in the public domain or publicly available and where disclosure may undermine the economic interest or competitive position of the owner of the information (HMA/EMA recommendations on transparency approved in November 2010 - Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation (EMA/484118/2010))

The final qualitative formulation (composition) of the authorised product is not commercially confidential.

In general, the names of manufacturers or suppliers of the active substance or the excipients are accepted as commercially confidential, unless disclosure is necessary for public health reasons (e.g. for some biological products).

2.1.2 Active substance

Detailed information on the synthesis or manufacture of the active substance, including details on the by-products and degradation products of active ingredients and validation of the manufacturing / synthesis process, is commercially confidential.

Information on the structure of the active substance is not commercially confidential. This will be known and published at the time of allocating the INN.

Detailed information concerning the particulars of studies regarding polymorphism and particle size should be treated as confidential.

Concerning impurities and degradation products, qualitative and quantitative information is regarded as confidential unless disclosure is necessary for public health reasons.

A general description of the types of test methods used and the appropriateness of the specification is not commercially confidential. However, detailed information on the test methods used and the specification and quantitative acceptance criteria established for the active substance is commercially confidential, unless the tests meet specific monographs in the European Pharmacopoeia or another National Pharmacopoeia.

In addition, for biotechnology products, a general description of the active ingredient including type of molecule and its general structural features (e.g. number of amino acids, general glycosylation details) or of the type of producer cell (e.g. E.Coli, S. Cerevisiae, Chinese Hamster Ovary cells, Madin Darby Kidney cells) is not considered commercially confidential. A general statement on the establishment of the Master Cell Bank (MCB) or Working Cell Bank (WCB) and on the stability of the cell banks is also not considered commercially confidential. General information on the fermentation and purification process is not commercially confidential, although details including operating parameters and specific material requirements are commercially confidential.

Details on the validation of the active substance manufacturing process are commercially confidential, although statements confirming that the manufacturing and control processes have been validated are not commercially confidential.

General information on the characterization of the active substance and statements confirming that the molecule is appropriately characterized are not considered commercially confidential. However, details of characterization methods are considered commercially confidential.

The above principles will also apply to novel excipients.

2.1.3 Finished product

The detailed descriptions of the manufacturing and control processes for the product are commercially confidential.

Details of the validation of the manufacturing process are also considered commercially confidential.

A general description of the types of test methods used and the appropriateness of the specification is not commercially confidential. Detailed information on the test methods included in the specification of the finished product and the quantitative acceptance criteria is commercially confidential, unless the tests are of Pharmacopoeial standard.

Concerning degradation products, qualitative and quantitative information is regarded as confidential unless disclosure is necessary for public health reasons.

Any confidentiality issue regarding novel packaging or medical device aspects should be justified by the applicant, and will be assessed according to the above principles.

2.2 Non-Clinical and Clinical Information

Information encompassing non-clinical and clinical development of the medicinal product and the subsequent assessment by Competent authorities is not *per se* commercially confidential. This includes information related to environmental risk assessments and risk management plans. Organisational information submitted as part of marketing authorisations procedures, e.g. the detailed description of a MAH's pharmacovigilance system, may be regarded as confidential, depending on the level of detail of the information provided.

With regard to the Assessment Report, this principle also applies regarding the outcome of discussion at the level of Competent Authorities' scientific committees or other scientific groups and to divergent opinions expressed within the scientific committees.

2.3 Information on Inspections

Information on the outcome of inspections (e.g. compliance/non-compliance/outstanding issues to be addressed) is not regarded as confidential, however specific details e.g. information regarding facilities and equipment are considered commercially confidential.

Any information available at EudraGMP can not be considered commercially confidential information considering it is already in the public domain.

3. Specific considerations on Personal Data Protection (PPD)

In regard to the disclosure of personal data enclosed in the MAA, the general principle should be redacting sensitive data details. Information on technical or professional qualifications should be disclosed in accordance with article 12 of Directive 2001/83/EC.

Any specific national legislation or national court decisions have to be followed.

3.1. Access to periodic safety update reports (PSURs) - Information on the personal data of individual persons

Right of access does not apply to information which reasonably could be traced back to individual persons.

This exception is relevant in relation to the line listings and case narratives of suspected adverse reactions reports in the PSURs recorded in the period in question. Therefore, before PSURs can be disclosed information on the health of natural persons, e.g. adverse drug reaction reports, which could be traced back to an individual person, have to be made anonymous.

The minimum personal data to be deleted to ensure anonymisation of the information would require the deletion of information on:

- 1) Date of birth
- 2) (Reporting) country
- 3) Patient identification code

In addition, case-by-case assessment should be made whether additional information should be deleted in any other part of the documentation of PSURs. This is particularly relevant concerning case narratives where much detailed personal information may appear.

It should never be possible to identify a natural person from the information disclosed, so in case of reports related to patients suffering from a rare disease it may be needed to delete further information.

GUIDANCE DOCUMENT ON THE IDENTIFICATION OF COMMERCIALLY CONFIDENTIAL INFORMATION AND PROTECTION OF PERSONAL DATA –
RELEASE OF INFORMATION AFTER GRANTING OF A MARKETING AUTHORISATION

STRUCTURE OF THE MARKETING AUTHORISATION DOSSIER
MODULE 1
Administrative information

APPLICATION – Cover Letter

	<p>Criteria – Can be released / Commercial Confidential Information (CCI) / case by case analysis (CBC) / Protection of Personal Data (PPD)</p> <p>Justification (when relevant)</p>
Name or company of the applicant in the EEA	CAN BE RELEASED
Home or office's headquarters of the applicant in the EEA	
Legal basis of the application	CAN BE RELEASED
Proposed (invented) name	<p>CAN BE RELEASED If the same as the final authorised name</p>
Documentation included in the process	CAN BE RELEASED

SUB-MODULE 1.1

INDEX - Comprehensive table of content	
Comprehensive index of Modules 1 to 5	CAN BE RELEASED Generally can be disclosed. Nevertheless, if the contents are detailed, in particular in Module 3, there might be CCI.
SUB-MODULE 1.2	
Application form	
Statement and signature	CAN BE RELEASED
Product (invented) name	CAN BE RELEASED for the final authorised name
Strength(s)	CAN BE RELEASED
Pharmaceutical form	
In accordance with <i>Standard Terms</i> (current version)	
Active Substance(s)	

Applicant	CAN BE RELEASED
Person authorised for communication on behalf of the applicant	
Original signature of the Applicant	
1. Type of application	
1.1. the application concerns	
1.1.1. centralised application	CAN BE RELEASED
1.1.2. mutual recognition procedure	
1.1.3. decentralised procedure	
1.1.4. national procedure	
1.2. Orphan medicinal product information	CAN BE RELEASED
1.3. is this application for a change to an extension	
No	CAN BE RELEASED
Yes	
qualitative change in declared active substance not defined as a new active substance	
Change of bioavailability	
Change of pharmacokinetics	
Change or addition of a new strength/potency	
change or addition of a new pharmaceutical form	
change or addition of a new route of administration	
For existing marketing authorisation in the Community / Member State where the application is made	
Name of the marketing authorisation holder	
Name, strength and pharmaceutical form	
Marketing authorisation number(s)	
1.4. Regulatory framework	
1.4.1. Article 8(3) application, (i.e. dossier with administrative, quality, pre-clinical and clinical data*)	CAN BE RELEASED
New active substance	
Known active substance	

1.4.2. Article 10(1) generic application	CAN BE RELEASED
Medicinal product which is or has been authorised in accordance with Community provisions in force for not less than 6/10 years in the EEA	
Evidence that the reference medicinal product which is or has been authorized for at least 6 / 10 years in the EEA, if necessary	
Medicinal product authorised in the Community/Member State where the application is made or European reference medicinal product	
Medicines used in the tests of BA / BE (if applicable)	
1.4.3. Article 10(3) hybrid application	CAN BE RELEASED
Medicinal product which is or has been authorised in accordance with Community provisions in force for not less than 6/10 years in the EEA	
Medicinal product authorised in the Community/Member State where the application is made or European reference medicinal product	
Medicinal product used in BA/BE studies (if applicable)	
Difference (s) compared to the reference medicinal product	
changes in the active substance(s)	
change in therapeutic indications	
change in pharmaceutical form	
change in strength (quantitative change to the active substance(s))	
change in route of administration	
bioequivalence can not be demonstrated through bioavailability studies	
1.4.4. Similar biological application	CAN BE RELEASED
1.4.5. Article 10a well-established use application	CAN BE RELEASED
Evidence that the active substance(s) have had a well-established use for at least 10 years	
1.4.6. Article 10b Fixed combination application	CAN BE RELEASED
1.4.7. Article 10c informed consent application	CAN BE RELEASED
<i>Authorised product in the Community / Member State where the application is made</i>	
Annex 5.2 – Attach letter of consent from the marketing authorisation holder of the authorised product (original document)	

2. MARKETING AUTHORISATION APPLICATION PARTICULARS	
2.1. Name(s) and ATC code	
2.1.1. Proposed (invented) name	CAN BE RELEASED for the final authorised name
2.1.2. Name of the active substance(s)	CAN BE RELEASED
2.1.3. Pharmacotherapeutic group (ATC code)	
2.2. Strength, pharmaceutical form, route of administration, container and pack sizes	
2.2.1 Pharmaceutical form	CAN BE RELEASED
use current list of standard terms (current version)	
2.2.1. Active substance(s)	
2.2.1. Strength(s)	
2.2.2. Route(s) of administration	
use current list of standard terms (current version)	
2.2.3. Container, closure and administration device(s)	
use current list of standard terms (current version)	
2.2.3.1. Package size(s)	
2.2.3.2. Proposed shelf life	
2.2.3.3. Proposed shelf life (after first opening container)	
2.2.3.4. Proposed shelf life (after reconstitution or dilution)	
2.2.3.5. Proposed storage conditions:	
2.2.3.6. Proposed storage conditions after first opening	
2.3. Legal status	
2.3.1. Proposed dispensing/classification	CAN BE RELEASED
subject to medical prescription	
not subject to medical prescription	
2.3.2. For products subject to medical prescription:	
product on prescription which may be renewed	
product on prescription which may not be renewed	

product on special prescription	
product on restricted prescription	
2.3.3. Supply for products not subject to medical prescription	
supply through pharmacies only	
supply through non-pharmacy outlets and pharmacies	
2.3.4. Promotion for products not subject to medical prescription	
promotion to health care professionals only	
promotion to the general public and health care professionals	
2.4. Marketing authorisation holder / Contact persons / Company	CAN BE RELEASED
2.4.1. Marketing authorisation holder	
Annex 5.3 – Proof of establishment of the applicant in the EEA	

2.4.2. Person/company authorised for communication on behalf of the applicant during the procedure in the Community/each MS	CAN BE RELEASED
Annex 5.4 - letter of authorisation for communication on behalf of the applicant/MAH.	
2.4.3. Person/Company authorised for communication between the marketing authorisation holder and the competent authorities after authorisation if different from 2.4.2 in the Community/each MS	
Annex 5.4 - letter of authorisation for communication on behalf of the applicant/MAH.	
2.4.4. Qualified person in the EEA for Pharmacovigilance	PPD See point 3 of the document
Annex 5.5 – Curriculum Vitae of the Qualified Person for Pharmacovigilance.	PPD See point 3 of the document
2.4.5. Scientific service of the MAH in the EEA	CAN BE RELEASED
2.5. Manufacturers	
2.5.1 Authorised manufacturer(s) (or importer(s)) responsible for batch release in the EEA	CAN BE RELEASED This information is publicly available in the PIL.

<p>Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)</p>	<p style="text-align: center;">CBC</p> <p>Considering that the name and address of the responsible for batch release is publicly available in the PIL and that Annex 1 and 2 of the Manufacturing Authorisation are public and available in EudraGMP, the document can be disclosed.</p> <p>Remaining annexes which are not available at EudraGMP and that may contain CCI should not be disclosed.</p>
<p>Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)</p>	<p style="text-align: center;">CAN BE RELEASED</p> <p>Considering that the name and address of the responsible for batch release is publicly available in the PIL and GMP certificate can be found in EudraGMP, therefore the document can be disclosed.</p>
<p>Annex 5.7 – Justification for more than one manufacturer responsible for batch release</p>	<p style="text-align: center;">CAN BE RELEASED</p>
<p>For medicinal products derived from blood and / or human plasma and vaccines, identification of the Official Medicines Control Laboratory (OMCL) where is the official batch release</p>	

2.5.1.1. Contact person in the EEA for product defects and recalls	<p style="text-align: center;">CBC</p> <p>See point 3 of the document</p>
2.5.1.2. Batch control Testing arrangements if different of 2.5.1.	<p style="text-align: center;">CBC</p> <p>When the Batch Control Testing Site and the Manufacturer Responsible for Batch Release are not the same or do not belong to the same group of companies, information should not be provided as it can disclose commercial agreements between different companies.</p>
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	<p style="text-align: center;">CBC</p> <p>Considering that the name and address of the responsible for batch release is publicly available in the PIL and that Annex 1 and 2 of the Manufacturing Authorisation are public and available in EudraGMP, the document can be disclosed.</p> <p>Remaining annexes which are not available at EudraGMP and that may contain CCI should not be disclosed.</p>

<p>Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)</p>	<p>CAN BE RELEASED</p> <p>Considering that the name and address of the responsible for batch release is publicly available in the PIL and GMP certificate can be found in EudraGMP, therefore the document can be disclosed.</p>
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2.5.2 Manufacturer(s) of the medicinal product and site(s) of manufacture	<p style="text-align: center;">CCI</p> <p>This information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>
Manufacturer of bulk	
<u>Site is in the EEA</u>	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA Site is outside the EEA with MRA agreement</u>	
Countries where MRA or other Community arrangements apply within the terms of the agreement	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA</u>	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	

Manufacturer responsible for primary packaging	<p>CCI</p> <p>This information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>
<u>Site is in the EEA</u>	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA with MRA agreement</u>	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA</u>	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
Manufacturer responsible for secondary packaging	
<u>Site is in the EEA</u>	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA Site is outside the EEA with MRA agreement</u>	

Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA</u>	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
Manufacturer of solvent / manufacturer of intermediate stage	<p style="text-align: center;">CCI</p> <p>This information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>
<u>Site is in the EEA</u>	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA</u>	
<u>Site is outside the EEA with MRA agreement</u>	
Annex 5.6 – Manufacturing Authorisation (if located in the EEA) or equivalent document (outside of the EEA where MRA or other Community arrangements apply) (document in the original language and the translation to English, if applicable)	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	
<u>Site is outside the EEA</u>	
Annex 5.9 – GMP certificate(s) (last inspection less than 3 years) (document in the original language and the translation to English, if applicable)	

<p>2.5.3. Manufacturer(s) of the active substance(s) and site(s) of manufacture</p>	<p>CCI / CAN BE RELEASED (biotechnological medicinal products)</p> <p>This information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p> <p>Exception: the manufacturers of biological substances are declared in the SPC in addition to the Manufacturer Responsible for Batch Release. After the marketing authorization or a variation, both the informations should be published as an abstract on the Official Journal as their public disclosure is necessary for the protection of public health.</p>
<p>Annex 5.8 – Flow-chart indicating all manufacturing and control sites involved in the manufacturing process of the medicinal product and the active substance</p>	<p>CCI</p> <p>This information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>

<p>Annex 5.22 *– For each active substance, attach a Statement(s) from the Qualified Person of the manufacturing authorisation holder in Section 2.5.1 and from the Qualified Person of each of the manufacturing authorisation holders (i.e. located in EEA) listed in Section 2.5.2 where the active substance is used as a starting material that the active substance is manufactured in compliance with the detailed guidelines on good manufacturing practice for starting materials. Alternatively, such Statement may be signed by one Qualified Person on behalf of all QPs involved (provided this is clearly indicated).</p> <p>* the existence of the GMP certificate for the manufacturer (s) (s) of substance (s) active (s) does not relieve the delivery of the statement</p>	<p style="text-align: center;">CCI</p> <p>Contains names of sites: this information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>
<p>Ph.Eur. Certificate of suitability</p>	
<p>Annex 5.10 – letter of access for Community/Member State authorities where the application is made</p>	
<p><i>Drug Master File (DMF)</i></p>	
<p>Annex 5.10 – copy of Ph. Eur. Certificate(s) of Suitability</p>	
<p>Annex 5.11 –Copy of written confirmation from the manufacturer of the active substance to inform the applicant in case of modification of the manufacturing process or specifications</p>	
<p>DMF number (if available)</p>	

2.5.4. Contract companies used for clinical trial(s) on bioavailability or bioequivalence	
Study sponsor	<p style="text-align: center;">CBC</p> <p>1. If the study name or medicinal product name used in the study mention the API manufacturer, this information must be considered as confidential</p> <p>2. If 1. is not applicable, the sponsor name must be provided since it is publicly available in EudraCT</p>
Study clinical center	<p style="text-align: center;">CCI</p> <p>This information is not publicly available in EudraCT</p>
Study analytical center	<p style="text-align: center;">CCI</p> <p>This information is not publicly available in EudraCT</p>
2.6 Qualitative and quantitative composition	
2.6.1. Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s)	<p style="text-align: center;">CAN BE RELEASED/CCI</p> <p>Partial suppression of information: the quantitative composition should be regarded as CCI since it reveals industrial secrecy.</p>
2.6.2. List of materials of animal and/or human origin contained or used in the manufacturing process of the medicinal product	<p style="text-align: center;">CCI</p>

Annex 5.12 – Ph. Eur. Certificate(s) of suitability for TSE	Might disclose information on the route of synthesis/manufacture process
2.6.3. Is an EMEA certificate for a Plasma Master File (PMF) issued	CCI
2.6.4. Does the medicinal product contain or consist of Genetically Modified Organisms (GMOs)	CAN BE RELEASED Information on GMO can not be confidential by law
3. SCIENTIFIC ADVICE	CAN BE RELEASED (Note: this section does not contain detailed information on scientific advice)

4. OTHER MARKETING AUTHORISATION APPLICATIONS	
4.1.1. Is there another Member State(s) where an application for the same* product is pending*	<p>CBC</p> <p>It can only be provided if the "pending" applications are already finalized in the other MS - need to consult the MS in question</p>
4.1.2. Is there another Member State(s) where an authorisation is granted for the same product	<p>CAN BE RELEASED</p>
4.1.3. Is there another Member State(s) where an authorisation was refused/ suspended/ revoked be released by competent authorities for the same* product	<p>CBC</p> <p>As in other situations, MS should be consulted.</p>
4.2. Marketing authorisation applications for the same product in the EEA	<p>CBC</p> <p>When the applicant and MAH are not the same or do not belong to the same group of companies, information should not be provided as it can disclose commercial agreements between different companies.</p> <p>It can only be provided if the "pending" applications are already finalized in the other MS - As in other situations, MS should be consulted.</p>
4.3. For multiple/duplicate applications of the same medicinal product	
4.4. Marketing authorisation applications for the same product outside the EEA	

5. ANNEXED DOCUMENTS (where appropriate)	
1. Proof of payment	CAN BE RELEASED
2. Informed consent letter of marketing authorisation holder of authorised medicinal product	
3. Proof of establishment of the applicant in the EEA.	
4. Letter of authorisation for communication on behalf of the applicant/MAH.	CBC When the applicant and MAH are not the same or do not belong to the same group of companies, information should not be provided as it can disclose commercial agreements between different companies.
5. Curriculum Vitae of the Qualified Person for Pharmacovigilance	PPD See point 3 of the document

<p>6. Manufacturing Authorisation required under Article 40 of Directive 2001/83/EC (or equivalent, outside of the EEA where MRA or other Community arrangements apply); any proof of authorisation in accordance with Article 8(k) of Directive 2001/83/EC</p>	<p style="text-align: center;">CBC/CCI</p> <p>CBC - For Manufacturer responsible for batch release</p> <p>Considering that the name and address of the manufacturer responsible for batch release is publicly available in the PIL and that Annex 1 and 2 of the Manufacturing Authorisation are public and available in EudraGMP, the document can be disclosed. Remaining annexes which are not available at EudraGMP and that may contain CCI should not be disclosed.</p> <p>CCI - For other manufacturers involved in the procedures</p> <p>(see 2.5 of the application form above)</p>
<p>7. Copy of the 'Qualification of SME Status</p>	<p style="text-align: center;">CAN BE RELEASED</p>
<p>8. Flow-chart indicating all manufacturing and control sites involved in the manufacturing process of the medicinal product and the active substance</p>	<p style="text-align: center;">CCI</p> <p>This information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>

<p>9. GMP certificate(s) or other GMP statement(s); Where applicable a summary of other GMP inspections performed</p>	<p align="center">CAN BE RELEASED/CCI</p> <p>CAN BE RELEASED - For Manufacturer responsible for batch release</p> <p>Considering that the name and address of the responsible for batch release is publicly available in the PIL and GMP certificate can be found in EudraGMP, therefore the document can be disclosed</p> <p>CCI - For other manufacturers involved in the procedures</p> <p>(see 2.5 of the application form above)</p>
<p>10. Letter(s) of access to Active Substance Master File(s) or copy of Ph. Eur. Certificate(s) of Suitability</p>	<p align="center">CCI</p>
<p>11. Copy of written confirmation from the manufacturer of the active substance to inform the applicant in case of modification of the manufacturing process or specifications according to Annex I of Directive 2001/83/EC.</p>	
<p>12. Ph. Eur. Certificate(s) of suitability for TSE</p>	

13. Written consent(s) of the competent authorities regarding GMO release in the environment.	<p align="center">CAN BE RELEASED</p> <p>Information on GMO can not be confidential by law.</p>
14. Scientific Advice given by CHMP and/or by member state(s)	<p align="center">CBC</p> <p>Depends on the content of the scientific advice given. (e.g. if the procedure is finalised and if the advice relates to the authorised indications, then the advice could be disclosed)</p>
15. Copy of Marketing Authorization(s) required under Article 8(j)-(L) of Directive 2001/83/EC in the EEA and the equivalent in third countries on request (a photocopy of the pages which give the marketing authorization number, the date of authorisation and the page which has been signed by the authorizing competent authority will suffice).	<p align="center">CAN BE RELEASED</p> <p>If procedures are finalised and considering that “photocopy of the pages which give the marketing authorization number, the date of authorisation and the page which has been signed by the authorizing competent authority will suffice”</p>
16. Correspondence with European Commission regarding multiple applications	<p align="center">CCI</p> <p>(EMA will inform that the request would be put forward to the EC)</p>
17. List of Mock-ups or Samples/specimens sent with the application, as appropriate (see Notice to Applicants, volume 2A, chapter 7)	<p align="center">CAN BE RELEASED</p>
18. Copy of the Orphan Designation Decision	<p align="center">CAN BE RELEASED</p>

19. List of proposed (invented) names and marketing authorisation holders in the concerned member states	<p align="center">CCI , except for the one authorised</p> <p>Invented names are not under trademark register protection, hence, can be considered as information with commercial value.</p>
20. Copy of EMEA certificate for a Vaccine Antigen Master File (VAMF).	<p align="center">CCI</p>
21. Copy of EMEA certificate for a Plasma Master File (PMF)	<p align="center">CCI</p>
22. For each active substance, attach a Statement(s) from the Qualified Person of the manufacturing authorisation holder in Section 2.5.1 and from the Qualified Person of each of the manufacturing authorisation holders (i.e. located in EEA) listed in Section 2.5.2 where the active substance is used as a starting material that the active substance is manufactured in compliance with the detailed guidelines on good manufacturing practice for starting materials. Alternatively, such Statement may be signed by one Qualified Person on behalf of all QPs involved (provided this is clearly indicated)	<p align="center">CCI</p> <p>Contains names of sites: this information refers to the manufacturing process and therefore, can reveal industrial secrecy.</p>

SUB-MODULE 1.3

Product Information	<p align="center">CAN BE RELEASED</p>
1.3.1. Summary of Product Characteristics, Package Leaflet and Labelling	
Summary of Product Characteristics (SPC)	

Labelling

primary packaging	CAN BE RELEASED
Secondary packaging	

Package Leaflet

1.3.2. Mock-up	CAN BE RELEASED
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1.3.3. SPECIMEN	CAN BE RELEASED
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1.3.4. READABILITY TESTING	CBC If a Readability Test/ Bridging Report is presented and only when the sponsor of the Test/ report and MAH are not the same or do not belong to the same group of companies, information should not be provided as it can disclose commercial agreements between different companies.
<i>Readability Testing</i>	
Justification for the failure to submit the test results of the readability test	

1.3.5. SPCs already approved in the Member States	CAN BE RELEASED
Copy of SPCs approved in other Member States	

1.3.6. BRAILLE	CAN BE RELEASED
Name of the medicinal product in <i>Braille</i>	

SUB-MODULE 1.4

Information about the Experts	PPD See point 3 of the document
1.4.1. Quality	
A Statement signed by the expert	
<i>A brief information (curriculum vitae) on the educational background, training and occupational experience of the expert (according to the Annex I of Directive 2001/83/EC).</i>	
1.4.2. Non-clinical	
A Statement signed by the expert	
<i>A brief information (curriculum vitae) on the educational background, training and occupational experience of the expert (according to the Annex I of Directive 2001/83/EC).</i>	
1.4.3. Clinical	
A Statement signed by the expert	
<i>A brief information (curriculum vitae) on the educational background, training and occupational experience of the expert (according to the Annex I of Directive 2001/83/EC).</i>	

SUB-MODULE 1.5

Specific Requirements for different types of applications	CAN BE RELEASED
1.5.1. Information for bibliographical applications	
1.5.2. Information for generic applications	
1.5.3. Market exclusivity	
1.5.4. Request in exceptional circumstances	
1.5.5. Conditional marketing authorization	

SUB-MODULE 1.6

Environmental risk assessment	CAN BE RELEASED
1.6.1. Non-OGM	
1.6.2. OGM	

SUB-MODULE 1.7

Information relating to Orphan Market Exclusivity	
1.7.1. Similarity	CBC This may include quality data that may need to be redacted as applied for module 3
1.7.2. Market Exclusivity	

SUB-MODULE 1.8

Information relating to Pharmacovigilance	
1.8.1. Pharmacovigilance System	CBC When the MAH and PhV QP do not belong to the same group of companies, information should not be provided as it can disclose commercial agreements between different companies. CBC analysis depending on the level of detail of the information
1.8.2. Risk-management System	CAN BE RELEASED

SUB-MODULE 1.9

Information relating to Clinical Trials	<p style="text-align: center;">CCI</p> <p>1. If the study name or medicinal product name used in the study mention the API manufacturer, this information must be considered as confidential</p> <p>2. If 1. is not applicable, the sponsor name must be provided since it is publicly available in EudraCT</p> <p>Study, clinical and analytical clinical centers are CCI (this information is not publicly available in EudraCT)</p>
A statement that the clinical trials performed outside the European Community meet the ethical requirements of the applicable legislation for clinical trials	

SUB-MODULE 1.10

Information relating to Paediatric

Applicants should therefore include the following documents in this section, as appropriate:

- copy of the product-specific waiver decision issued by the EMA;

or

- copy of the class-waiver decision issued by the EMA;

or

- copy of the latest version of the PIP Decision(s) (incl. deferrals, if applicable), together with

-if available-:

- A copy of the PDCO opinion on PIP compliance + report (in case PIP compliance verification by PDCO has taken place)

- The applicant's "PIP Compliance Report" (in case no competent authority compliance verification has taken place). Please also refer to the Template for

such PIP compliance reports published on the EMA website (include link to doc on Website once published). Related study reports should be placed in the

relevant Modules of the dossier and cross-referred to accordingly.

- Overview table of the PIP results, indicating in which application(s) they were/are going to be submitted, status of the application(s), as well as their

location in the present application.

CBC

Documents published at the EMA's website can be disclosed. Other documents should be further analysed in a *case by case* basis, in order to decide if they can be disclosed or not. If the procedure is finalised and if it is related to the same indications, then **"CAN BE RELEASED"**.

MODULE 2

Summary/Overview

SUB-MODULE 2.1

INDEX	
Overall CTD Table of Contents of Modules 2, 3, 4, and 5	CBC Generally can be disclosed. Nevertheless, if the contents are detailed, in particular in Sub-module 2.3, there might be CCI.

SUB-MODULE 2.2

Introduction	CAN BE RELEASED
Pharmacological group	
Mode of action and proposed clinical use	

SUB-MODULE 2.3

Quality Overall Summary	CBC Can only be disclosed information on: nomenclature, structure and general properties of the active substance (2.3.S.1). Also, qualitative composition on the medicinal product can be disclosed (2.3.P.1).
Report of the chemical, pharmaceutical and biological data	
Active substance	CCI
Finished product	

SUB-MODULE 2.4

Non-clinical Overview	CAN BE RELEASED
Report on Non-clinical data	

SUB-MODULE 2.5

Clinical Overview	CAN BE RELEASED
Report on clinical data	

SUB-MODULE 2.6

Non-clinical Summary	CAN BE RELEASED NOTE: this information can be considered sensitive (related with animal protection issues)
2.6.1. Pharmacology Written Summary	
2.6.2. Pharmacology Tabulated Summary	
2.6.3. Pharmacokinetics Written Summary	
2.6.4. Pharmacokinetics Tabulated Summary	
2.6.5. Toxicology Written Summary	
2.6.6. Toxicology Tabulated Summary	
2.6.7. Summary toxicology in tabular format	

SUB-MODULE 2.7

Clinical Summary	
2.7.1. Summary of biopharmaceutics and associated analytical methods	CAN BE RELEASED 2.7.5. - the list of references can be disclosed but not the references themselves because of copyright.
2.7.2. Summary of clinical pharmacology studies	
2.7.3. Summary of clinical efficacy	
2.7.4. Summary of clinical safety	
2.7.5 References	
2.7.6. Synopses of Individual Studies	CAN BE RELEASED

**MODULE 3
QUALITY****SUB-MODULE 3.1**

INDEX	
MODULE 3 TABLE OF CONTENTS	CBC Generally can be disclosed. Nevertheless, if the contents are detailed, there might be CCI.

SUB-MODULE 3.2

3.2.S – Active substance	CAN BE RELEASED
3.2.S.1 – General Information	
3.2.S.1.1 – Nomenclature	
3.2.S.1.2 – Structure	CCI This information refers to the manufacturing process of the active substance and therefore, can reveal industrial secrecy.
3.2.S.1.3 – General Properties	
3.2.S.2. – Manufacture	
3.2.S.2.1 – Manufacturer(s)	
3.2.S.2.2 – Description of manufacturing process and process controls	
3.2.S.2.3 – Control of materials	
3.2.S.2.4 – Controls of critical steps and intermediates	
3.2.S.2.5 – Process validation and/or evaluation	
3.2.S.2.6 – Manufacturing process development	
3.2.S.3. – Characterisation	
3.2.S.3.1 – Elucidation of structure and other characteristics	
3.2.S.3.2 – Impurities	
3.2.S.4. – Control of drug substance	
3.2.S.4.1 – Specification	
3.2.S.4.2 – Analytical Procedures	
3.2.S.4.3 – Validation of analytical procedures	
3.2.S.4.4 – Batch analyses	
3.2.S.4.5 – Justification of Specification	
3.2.S.5. – Reference Standards or Materials	
3.2.S.6. – Container Closure System	
3.2.S.7. – Stability	

3.2.P – DRUG PRODUCT	
3.2.P.1 – Description and composition of the drug product	CAN BE RELEASED/CCI Partial suppression of information: the quantitative composition should be regarded as CCI since it reveals industrial secrecy.
3.2.P.2 – Pharmaceutical Development	CCI This information refers to the manufacturing process of the medicinal product and therefore, can reveal industrial secrecy.
3.2.P.3 - Manufacture	
3.2.P.3.1 – Manufacturer(s)	
3.2.P.3.2 – Batch formula	
3.2.P.3.3 – Description of Manufacturing Process and Process Controls	
3.2.P.3.4 – Controls of critical steps and intermediates	
3.2.P.3.5 – Process validation and / or evaluation	
3.2.P.4. – Control of excipients	CCI This information refers to the manufacturing process of the medicinal product and therefore, can reveal industrial secrecy.
3.2.P.4.1 – Specifications	
3.2.P.4.2 – Analytical procedures	
3.2.P.4.3 – Validation of analytical procedures	
3.2.P.4.4 – Justification of specifications	
3.2.P.4.5 – Excipients of human or animal origin	
3.2.P.4.6 – Novel Excipients (<i>ref to A 3</i>)	
3.2.P.5 – Control of drug product	
3.2.P.5.1 – Specification(s)	
3.2.P.5.2 – Analytical Procedures	
3.2.P.5.3 – Validation of Analytical Procedures	
3.2.P.5.4 – Batch analyses	
3.2.P.5.5 – Characterisation of Impurities	
3.2.P.5.6 – Justification of specification(s)	
3.2.P.6 – Reference Standards or Materials	
3.2.P.7 – Container Closure System	
3.2.P.8 – Stability	

3.2.A – APPENDICES	
3.2.A.1 – Facilities and Equipment (biological medicinal products only)	
3.2.A.2 – Adventitious Agents Safety Evaluation	
3.2.A.3 – new Excipients	
3.2.R – Additional information for the European Community (REGIONAL INFORMATION)	
Process validation Scheme for the Drug Product	
Medical device	
Certificate(s) of Suitability	
Medicinal products containing or using in the manufacturing process materials of animal and/or human origin	

SUB-MODULE 3.3

LITERATURE REFERENCES	CAN BE RELEASED (only the list of references due to copyright)
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MODULE 4
NONCLINICAL STUDY REPORTS

SUB-MODULE 4.1

INDEX	
MODULE 4 TABLE OF CONTENT	CAN BE RELEASED

SUB-MODULE 4.2

STUDY REPORTS	CAN BE RELEASED
4.2.1 PHARMACOLOGY	
4.2.1.1 Primary pharmacodynamics	
4.2.1.2 Secondary pharmacodynamics	
4.2.1.3 Safety pharmacology	
4.2.1.4 Pharmacodynamic drug interactions	PPD personal data relating to investigators should follow the instructions in section 3
4.2.2 PHARMACOKINETICS	
4.2.2.1 Analytical Methods and Validation Reports	

4.2.2.2 Absorption	CAN BE RELEASED
4.2.2.3 Distribution	
4.2.2.4 Metabolism	
4.2.2.5 Excretion	
4.2.2.6 Pharmacokinetic Drug Interactions (nonclinical)	
4.2.2.7 Other Pharmacokinetic Studies	
4.2.3 TOXICOLOGY	
4.2.3.1 Single-dose toxicity	
4.2.3.2 Repeat-dose toxicity	
4.2.3.3 Genotoxicity <i>in vitro</i> e <i>in vivo</i>	
4.2.3.4 Carcinogenicity	
4.2.3.5 Reproductive and developmental toxicity	
4.2.3.6 Local tolerance	
4.2.3.7 Other toxicity studies	

SUB-MODULE 4.3

LITERATURE REFERENCES	CAN BE RELEASED (only the list of references due to copyright)
LITERATURE REFERENCES	

**MODULE 5
CLINICAL STUDY REPORTS**

SUB-MODULE 5.1

INDEX	CAN BE RELEASED
MODULE 5 TABLE OF CONTENTS	

SUB-MODULE 5.2

TABULAR LISTINGS OF ALL CLINICAL STUDIES	CAN BE RELEASED
TABULAR LISTINGS	

SUB-MODULE 5.3

CLINICAL STUDY REPORTS	CBC This section may contain information on bio analytical methods developed/owned (and not publicly available) by the sponsor or CRO. Such information may be confidential.
5.3.1 Reports of Biopharmaceutic and Bioavailability (BA) Studies	PPD Personal data should follow the instructions in section 3
5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	

5.3.3 Reports of human pharmacokinetic (PK) studies	PPD Personal data should follow the instructions in section 3
5.3.4 Reports of human pharmacodynamic (PD) studies	PPD, Personal data should follow the instructions in section 3
5.3.5 Reports of efficacy and safety studies	
5.3.6 Reports of post-marketing experience	
5.3.7 Case report forms and individual patient listings, when submitted	

SUB-MODULE 5.4

LITERATURE REFERENCES	CAN BE RELEASED (only the list of references due to copyright)
More information	