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

In November 2010 HMA and EMA agreed to lay down a common approach on what should be considered as commercially confidential (see HMA/EMA recommendations on transparency - EMA/484118/2010). The objective was to facilitate a common and consistent approach across the European Economic Area (EEA) to provide guidance on the identification of commercially confidential information or on personal data that must be protected, provided in the Marketing Authorisation (MA) dossier after a MA is granted, when dealing with request of access to documents at EEA level.

This guidance document is intended to be applicable to information requests on medicinal products authorised 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.

When it comes to disclosure, the decision lies with the regulatory authorities. Efforts can be made to inform or consult the Marketing Authorisation Holder (MAH) prior to responding to a request of access to documents. This will depend on national legal frameworks.

This guidance addresses the approach to provide access to different information in the MA dossier as high-level principles and follows the structure of the Common Technical Document (CTD). However, the remit of the principles outlined should only be applicable to dossiers for authorised medicinal products. Other type of applications or parts of dossiers such as orphan designations and paediatric investigation plans are not intended to be covered by the principles laid out in this guidance document, neither those withdrawn or rejected.

This guidance document is intended to be a consensus document agreed by the whole Network of National Competent Authorities of the EEA for the release of information regarding medicinal products for human use (i.e. not applicable to medicinal products for veterinary use) and lays 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 /European legislation in terms of access to documents and on the protection of personal data (based on the Directive 95/46/EC). Also, in cases of an overriding public health reason, regulatory authorities may disclose information normally classified as Commercially Confidential Information throughout this guidance document if their legislation so provides.

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 Information): means that the section contains commercially confidential information **and therefore, as a main rule, cannot be released (the corresponding section of the CTD has to be redacted).** 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)).

PPD (Protected Personal Data): means that the section may contain personal data **that have to be protected** and **therefore, as a main rule, cannot be released or should be redacted before release**. Definition from Directive 95/46/EC: "Personal data" shall mean any information relating to an identified or identifiable natural person ('data subject'); an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity.

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

CBR (Can Be Released): means that all of the section can be released, always after preliminary review.

2. Principles on Protection of Personal Data (PPD)

The following principles have been agreed and the designation indicated is subject to the provisions listed:

HMA/EMA considers that very little information in the application dossier should be considered as personal data that should be protected from disclosure. Personal data in the dossier mainly falls into the following categories:
A. Personal data relating to experts or designated personnel included in the dossier.
B. Personal data relating to other staff included in the dossier.
C. Personal data related to patients included in clinical trial study reports.
D. Personal data related to pharmacovigilance information on individual patients.

Notwithstanding specific national legislation, the following policy will be applied to the four categories identified above.

A. Personal data related to experts or designated personnel - CBR[1]:
In general, it is considered that names of experts or designated personnel with legally defined responsibilities and roles with respect to aspects of the Marketing Authorisation dossier (e.g. QP, QPPV, Clinical expert, Investigator) are included in the dossier because they have a legally defined role or responsibility and it is in the public interest to release this data.
Applicants are advised that non-essential information (e.g. personal address, personal phone number) should not be included in the dossier.

[1] Some Member States have specific legislation and/or specific national rules, guidances or practices on the protection of personal data and therefore, in these countries, this data may be redacted.

For dossiers prepared before the application of this guidance document, such personal data will be redacted only if disclosure could lead to infringement of personal integrity or cause personal harm.
EMA/HMA aims to work with stakeholders to develop a plan to ensure that such data will no longer be included from an agreed date.

In addition, certain competent authorities may redact names of experts involved in animal studies where it can be considered that disclosure of such information may present a security risk to those individuals in the country concerned.

B. Personal data relating to other staff included in the dossier - PPD if included:
HMA/EMA does not consider that names or personal details of other staff need to be included in the dossier. Applicants are therefore advised that such data should not be included in the dossier.

For dossiers prepared before the application of this guidance document, such personal data will be redacted.

EMA/HMA aims to work with stakeholders to develop a plan to ensure that such data will no longer be included from an agreed date.

C. Personal data related to patients included in clinical trial study reports - PPD if included:

The current European legislation requires patient information to be included in non-identifiable form in the marketing authorisation application submitted to competent authorities. Therefore, applicants should ensure that the dossiers submitted meet legislative requirements. The applicant remains responsible for compliance with the legislation in cases where such data is inadvertently included in the dossier.

D. Personal data related to pharmacovigilance information on individual patients – PPD:

Although it is not expected that much pharmacovigilance information related to individual patients will be provided as part of the initial MAA, this cannot be excluded. In addition a request may cover an application in the post-authorisation phase.
In this case the principles outlined in the HMA/EMA recommendations on the handling of requests for access to period safety update reports EMEA/74133/2009 will be applied. Where necessary at least dates of birth, reporting country information and patient identification code will be redacted before release.
Any specific national legislation or national court decisions have to be followed.

2.1. Signatures
The release of signatures of experts or designated personnel in the dossier should take into consideration the specific national legislation and practices and should follow a case-by-case approach.

2.2. 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.

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

These principles apply both to the granting of access to the MA dossier after approval 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 parts 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.

3.1 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.

3.1.1 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).

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).

3.1.2 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 Pharmacopeia.

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.

3.1.3 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.

3.2. 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. In general, the data included in clinical trial study reports is considered as data that can be released as such data is not considered either commercially confidential or personal data that should be protected. In the case of exceptional and substantiated cases, particularly where innovative study designs and/or innovative analytical methods have been used, consideration will be given to the need for redaction.
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.

3.3 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.

3.4. Contractual agreements

Contractual agreements between companies are generally considered Commercially Confidential Information, excluding the contracts between companies and Contract Research Organisations (CROs), are excluded. With regard to information in modules 4 and 5 of the dossier, it is considered that contractual information with companies responsible for non-clinical and clinical studies, including CROs, can be released as they may contribute to and be responsible for important information included in the dossier. The names of these CROs are therefore considered as information which can be released (CBR).

3.5. Scientific advice

The release of information on an agreed therapeutical indication should not be regarded as Commercially Confidential Information after the conclusion of the procedure. However, all the information related with new developments and formulations should be protected.

3.6. Pharmacovigilance information

Since pharmacovigilance legislation is currently being implemented, we defer this discussion until this work has been completed.

3.7. List of references and original manuscripts

The list of references of the publications included in the dossier is not considered as confidential and can be released.

However, if the actual manuscripts are included, these may be subject to copyright. If there is no copyright, the manuscripts may be released upon request.

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

STRUCTURE OF THE MARKETING AUTHORISATION DOSSIER
MODULE 1
Administrative information

APPLICATION – *Cover Letter*

Cover letter as such	**CBC** Content of cover letters vary widely, so redaction depends on actual content of the cover letter; some guidance is identified below
Name or company of the applicant in the EEA	**CBC** In accordance with principles 2.A and 3.4 outlined above.
Home or office's headquarters of the applicant in the EEA	
Legal basis of the application	**CBR**
Proposed (invented) name	**CBC** Invented names can be considered as information with commercial value. **CBR** only, if the same as the final authorised name.
Signature	**CBC** In accordance with principle 2.1 outlined above.

SUB-MODULE 1.1

INDEX - Comprehensive table of content	
Comprehensive index of Modules 1 to 5	**CBC** Generally can be disclosed. Nevertheless, if the contents are too detailed, in particular in Sub-module 2.3 and Module 3, there might be **CCI**.
SUB-MODULE 1.2	
Application form	
Statement and signature	**CBC** In accordance with principles 2.A and 2.1 outlined above.
Product (invented) name	**CBC** Invented names can be considered as information with commercial value. CBR only, if the same as the final authorised name
Strength(s)	**CBR**
Pharmaceutical form	
In accordance with *Standard Term*s (current version)	
Active Substance(s)	
Applicant	
Person authorised for communication on behalf of the applicant	
Original signature of the Applicant	**CBC** In accordance with principle 2.1 outlined above

1.Type of application	
1.1. the application concerns	
1.1.1. centralised application	**CBR**
1.1.2. mutual recognition procedure	
1.1.3. decentralised procedure	
1.1.4. national procedure	
1.2. Orphan medicinal product information	
1.3. is this application for a change to an extension	
No	
Yes	
qualitative change in declared active substance not defined as a new active substance	
Change of bioavailability	
Change of pharmacinetics	
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*)	
New active substance	
Known active substance	

1.4.2. Article 10(1) generic application	**CBR**
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	
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	
1.4.5. Article 10a well-established use application	
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	
1.4.7. Article 10c informed consent application	
Authorised product in the Community / Member State where the application is made	

2. **MARKETING AUTHORISATION APPLICATION PARTICULARS**	
2.1. Name(s) and ATC code	
2.1.1. Proposed (invented) name	**CBC** Invented names can be considered as information with commercial value. **CBR** <u>only</u>, if the same as the final authorised name
2.1.2. Name of the active substance(s)	**CBR**
2.1.3. Pharmacotherapeutic group (ATC code)	
2.2. Strength, pharmaceutical form, route of administration, container and pack sizes	
2.2.1 Pharmaceutical form	**CBR**
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	**CBR**
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	
2.4.1. Marketing authorisation holder	**CBR**

2.4.2. Person/company authorised for communication on behalf of the applicant during the procedure in the Community/each MS	**CBC** If this person/company belongs to the staff or are the same as the MAH, this information should be regarded as **CBR**. If, not, this information should be regarded as **CCI** which is in accordance with the principle 3.4 outlined above.
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**	
2.4.4. Qualified person in the EEA for Pharmacovigilance	**CBR** In accordance with principle outlined above: 2.A.
2.4.5. Scientific service of the MAH in the EEA	**CBC** In accordance with principles outlined above: 2.A and 3.4. above.
2.5. Manufacturers	
2.5.1 Authorised manufacturer(s) (or importer(s)) responsible for batch release in the EEA	**CBR** This information is publicly available in the PIL.
2.5.1.1. Contact person in the EEA for product defects and recalls	**CBC** In accordance with principles outlined above: 2.A and 3.4.

2.5.1.2. Batch control Testing arrangements if different of 2.5.1.	**CBC** When the Batch Control Testing Site and the MAH are not the same or do not belong to the same group of companies, information should be regarded as CCI which is in accordance with the principle 3.4 outlined above.
2.5.2 Manufacturer(s) of the medicinal product and site(s) of manufacture	**CCI** In accordance with principles 3.1.3 and 3.4 outlined above.

2.5.3. Manufacturer(s) of the active substance(s) and site(s) of manufacture	**CCI** In accordance with principles 3.1.2 and 3.4 outlined above. **Exception (CBR):** the manufacturers of biological substances are declared in the Annex II to the MA in addition to the Manufacturer Responsible for Batch Release. After the marketing authorisation or a variation the information should be published as an abstract in the Official Journal.

2.5.4. Contract companies used for clinical trial(s) on bioavailability or bioequivalence	
Study sponsor	**CBC** **1.** If the study name or medicinal product name used in the study mention the API manufacturer, this information must be considered as CCI which is in accordance with principles 3.1.2 and 3.4 outlined above. **2.** If **1.** is not applicable, the sponsor name must be regarded as **CBR** which is in accordance with the principle 3.4 outlined above.
Study clinical center	**CBR** In accordance with the principle 3.4 outlined above.
Study analytical center	**CBR** In accordance with the principle 3.4 outlined above.

2.6 Qualitative and quantitative composition	
2.6.1. Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s)	**CBR/CCI** The qualitative composition on the medicinal product (i.e. only the composition as described in section 6.1 of the SPC, that is publicly available in product information) can be disclosed but the quantitative composition should be regarded as **CCI** since it reveals industrial secrecy. This is in accordance with the principles outlined above: 3.1.1 and 3.1.3
2.6.2. List of materials of animal and/or human origin contained or used in the manufacturing process of the medicinal product	**CCI** Might disclose information on the route of synthesis/manufacture process. Hence in accordance with principles 3.1.2, 3.1.3 and 3.4 outlined above, should be regarded as CCI.
2.6.3. Is an EMA certificate for a Plasma Master File (PMF) issued	**CCI**
2.6.4. Does the medicinal product contain or consist of Genetically Modified Organisms (GMOs)	**CBR** Information on GMO can not be confidential by law
3. SCIENTIFIC ADVICE	**CBR** **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*	**CBC** It can only be provided if the pending applications are already finalized in the other MS - need to consult the MS in question.
4.1.2. Is there another Member State(s) where an authorisation is granted for the same product	**CBR**
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	**CBC** As in other situations, MS should be consulted.
4.2. Marketing authorisation applications for the same product in the EEA	**CBC** It can only be provided if the "pending" applications are already finalized in the other MS - As in other situations, MS should be consulted.
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	**CBC** In accordance with principle 2.1 outlined above.
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** In accordance with principles 2.A. and 3.4 outlined above. Principle 2.1. also applies as the letter should be signed.
5. Curriculum Vitae of the Qualified Person for Pharmacovigilance	**CBC** In accordance with principles 2.A and 2.1 outlined above

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	**CBR/CCI** **For Manufacturer responsible for batch release - CBR** 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 de disclosed. **Note**: remaining annexes which are not available at EudraGMP and that may contain **CCI** should not be disclosed. **For other manufacturers involved in the procedures – CCI** In accordance with principles 3.1.3 and 3.4 outlined above.
7. Copy of the 'Qualification of SME Status	**CBR**
8. Flow-chart indicating all manufacturing and control sites involved in the manufacturing process of the medicinal product and the active substance	**CCI** In accordance with principles 3.1.2, 3.1.3 and 3.4 outlined above.

9. GMP certificate(s) or other GMP statement(s); Where applicable a summary of other GMP inspections performed	**CBR/CCI** **For Manufacturer responsible for batch release - CBR** 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. In accordance with principle 3.3 outlined above. **For other manufacturers involved in the procedures - CCI** In accordance with principles 3.1.2, 3.1.3, 3.3 and 3.4 outlined above.
10. Letter(s) of access (LoA) to Active Substance Master File(s) or copy of Ph. Eur. Certificate(s) of Suitability	**CCI** Contains names of sites. Hence, in accordance with principles 3.1.2 and 3.4 outlined above should be regarded as **CCI**. Also, the principle 2.1 applies both in the case of LoA and LoC.
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 (letter of commitment - LoC).	

12. Ph. Eur. Certificate(s) of suitability for TSE	**CCI** Might disclose information on the route of synthesis/manufacture process. Hence in accordance with principles 3.1.2, 3.1.3 and 3.4 outlined above, should be regarded as **CCI**.

13. Written consent(s) of the competent authorities regarding GMO release in the environment.	**CBR** Information on GMO can not be confidential by law.
14. Scientific Advice given by CHMP and/or by member state(s)	**CBC** Depends on the content of the scientific advice given. The principle 3.5 outlined above should be followed.
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).	**CBR** 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”.

16. Correspondence with European Commission regarding multiple applications	**CBC** This letter might contain extensive sensitive information on contractual arrangements (principle 3.4).
17. List of Mock-ups or Samples/specimens sent with the application, as appropriate (see Notice to Applicants, volume 2A, chapter 7)	**CBR**
18. Copy of the Orphan Designation Decision	**CBR**
19. List of proposed (invented) names and marketing authorisation holders in the concerned member states	**CBC** Invented names can be considered as information with commercial value. **CBR** only, if the same as the final authorised name.
20. Copy of EMEA certificate for a Vaccine Antigen Master File (VAMF).	**CCI**
21. Copy of EMEA certificate for a Plasma Master File (PMF)	**CCI**
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)	**CCI** Statement(s) contains names of sites. Hence in accordance with principles 2.1, 3.1.2 and 3.4 outlined above, should be regarded as **CCI**.

SUB-MODULE 1.3

Product Information	**CBR**
1.3.1. Summary of Product Characteristics, Package Leaflet and Labelling	
Summary of Product Characteristics (SPC)	

Labelling

primary packaging	**CBR**
Secondary packaging	

Package Leaflet

1.3.2. Mock-up	**CBR**

1.3.3. SPECIMEN	**CBR**

1.3.4. READABILITY TESTING	**CBC**
Readability Testing	
Justification for the failure to submit the test results of the readability test	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, which is in accordance with principle 3.4 above.

1.3.5. *SPCs already approved in the Member States*	**CBR**
Copy of SPCs approved in other Member States	

1.3.6. BRAILLE	**CBR**
Name of the medicinal product in *Braille*	

SUB-MODULE 1.4

Information about the Experts	**CBC**
1.4.1. **Quality**	In accordance with principles 2.A and 2.1 above.
A Statement signed by the expert	
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).	
1.4.2. **Non-clinical**	
A Statement signed by the expert	
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).	
1.4.3. **Clinical**	
A Statement signed by the expert	
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).	

SUB-MODULE 1.5

Specific Requirements for different types of applications	**CBR**
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	**CBR**
1.6.1. Non-GMO	In general, information on ERA in the human medicines fields is not confidential.
1.6.2. GMO	

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 in accordance with principles 3.1.1, 3.1.2 and 3.1.3.
1.7.2. **Market Exclusivity**	

SUB-MODULE 1.8

Information relating to Pharmacovigilance	
1.8.1. Pharmacovigilance System	Please refer to principle 3.6 above.
1.8.2. Risk-management System	

SUB-MODULE 1.9

Information relating to Clinical Trials	**CBC**
A statement that the clinical trials performed outside the European Community meet the ethical requirements of the applicable legislation for clinical trials	**1.** If the study name or medicinal product name used in the study mention the API manufacturer, this information must be considered as **CCI** which is in accordance with principles 3.1.2 and 3.4 outlined above. **2.** If **1.** is not applicable, the statement must be regarded as **CBR** which is in accordance with the principle 3.4 outlined above. Nevertheless, the principle 2.1 should be borne in mind.

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 **CBR**.

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	**CBR**
Pharmacological group	
Mode of action and proposed clinical use	

SUB-MODULE 2.3

Quality Overall Summary	**CBC** Information on: nomenclature, structure and general properties of the active substance (2.3.S.1) and qualitative composition on the medicinal product (2.3.P.1) **CBR**. All the remaining information should be regarded as **CCI** which is in accordance with principles outlined above: 3.1., 3.1.1, 3.1.2 and 3.1.3.
Report of the chemical, pharmaceutical and biological data	
Active substance	
Finished product	

SUB-MODULE 2.4

Non-clinical Overview	**CBR**
Report on Non-clinical data	In accordance with principles outlined above: 2.A, 2.1 and 3.2.

SUB-MODULE 2.5

Clinical Overview	**CBR**
Report on clinical data	In accordance with principle 3.2.. However, in accordance with principles 2.A, 2.B, 2.C and 2.1 some information in this section may be regarded as **PPD**.

SUB-MODULE 2.6

Non-clinical Summary	**CBR** In accordance with principles outlined above: 2.A, 2.1 and 3.2.
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	**CBR** In accordance with principle 3.2. However, in accordance with principles 2.A, 2.B, 2.C and 2.1, some information in this section may be regarded as **PPD**.
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	**CBR** In accordance with the principle outlined above: 3.7
2.7.6. Synopses of Individual Studies	**CBR** In accordance with principle 3.2.. However, in accordance with principles 2.A, 2.B and 2.C some information in this section may be regarded as **PPD**.

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** in accordance with principle 3.1 outlined above.

SUB-MODULE 3.2

3.2.S – Active substance	
3.2.S.1 – General Information	**CBR** This section should be generally classified as CBR, however and only
3.2.S.1.1 – Nomenclature	
3.2.S.1.2 – Structure	
3.2.S.1.3 – General Properties	

	if it contains detailed information regarding new biologic active substances belonging to the class of recombinant proteins/polypeptides that reveals a trade secret (not patented), information on the amino acid sequence, should be regarded as CCI. This is in accordance with the principle outlined above: 3.1.2.

3.2.S.2. – Manufacture	**CCI** In accordance with principle outlined above: 3.1.2.
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**	**CBR/CCI** The qualitative composition on the medicinal product (*i.e.* only the composition as described in section 6.1 of the SPC, that is publicly available in product information) can be disclosed but the quantitative composition should be regarded as CCI since it reveals industrial secrecy**.** This is in accordance with the principles outlined above: 3.1.1 and 3.1.3
3.2.P.2 – Pharmaceutical Development	**CCI** In accordance with principle outlined above: 3.1.1. and 3.1.3.
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	
3.2.P.4.1 – Specifications	**CCI** In accordance with principle outlined above: 3.1.1. and 3.1.3.
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 *(ref to A 3)*	
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	**CCI** In accordance with principle outlined above: 3.1.1., 3.1.2 and 3.1.3.
3.2.A.1 – Facilities and Equipment (biological medicinal products only)	
3.2.A.2 – Adventitious Agents Safety Evaluation	
3.2.A.3 – news 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	**CBR** In accordance with the principle outlined above: 3.7

MODULE 4
NONCLINICAL STUDY REPORTS

SUB-MODULE 4.1

INDEX	
MODULE 4 TABLE OF CONTENT	**CBR**

SUB-MODULE 4.2

STUDY REPORTS	**CBR** In accordance with principles outlined above: 2.A, 2.1 and 3.2.
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	
4.2.2 **PHARMACOKINETICS**	
4.2.2.1 Analytical Methods and Validation Reports	
4.2.2.2 Absorption	
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 *in vitro* e *in vivo*	
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	**CBR** In accordance with the principle outlined above: 3.7

MODULE 5
CLINICAL STUDY REPORTS

SUB-MODULE 5.1

INDEX	**CBR**
MODULE 5 TABLE OF CONTENTS	

SUB-MODULE 5.2

TABULAR LISTINGS OF ALL CLINICAL STUDIES	**CBR**
TABULAR LISTINGS	In accordance with the principle outlined above: 3.2 and 3.7

CLINICAL STUDY REPORTS	**CBR**
5.3.1 Reports of Biopharmaceutic and Bioavailability (BA) Studies	
5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	However, 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. This is in accordance with the principle 3.2. outlined above.

SUB-MODULE 5.3

CLINICAL STUDY REPORTS	**CBR** However, this section may contain information on bio analytical methods developed/owned (and not publicly available) by the sponsor or CRO. Such information may be regarded as **CCI**. This is in accordance with the principle 3.2.outlined above. If not, this section should be regarded as **CBR,** this is in accordance with the principles 3.2. and 3.4 outlined above In accordance with principles 2.A, 2.B, 2.C and 2.1, some information in this section may be regarded as **PPD**.
5.3.1 Reports of Biopharmaceutic and Bioavailability (BA) Studies	
5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	
5.3.3 Reports of human pharmacokinetic (PK) studies	
5.3.4 Reports of human pharmacodynamic (PD) studies	
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	**CBR** In accordance with the principle outlined above: 3.7