To: European Commission
DG SANCO/Pharmaceuticals
sanco-pharmaceuticals@ec.europa.eu

janssen
PHARMACEUTICAL COMPANIES
OF Johnson&Johnson

7th November 2011

Dear Sirs,

Response of Janssen, Pharmaceutical Companies of Johnson & Johnson, to the "PCIM/11/01 – Public Consultation on implementing measures for pharmacovigilance"

Janssen, Pharmaceutical Companies of Johnson & Johnson (hereafter "Janssen") welcomes the Concept Paper submitted for public consultation on the 'Implementing Measures in Order to Harmonise the Performance of the Pharmacovigilance Activities Provided for in Directive 2001/83/EC and Regulation (EC) No 726/2004' and would like to thank the European Commission for the opportunity to comment.

As implementation of the new pharmacovigilance legislation in European Union (EU) will redefine the way we monitor our products and ultimately the safety of our patients, Janssen has a major interest in the topics covered by the Concept Paper provided by the European Commission.

In response to the questions presented in the Concept Paper, our comments are provided below:

A. Pharmacovigilance System Master File

Consultation item no. 1: Should additional processes and pharmacovigilance tasks be covered?

No additional processes or pharmacovigilance tasks need to be covered in the pharmacovigilance system master file.

Consultation item no. 2: The aim of the pharmacovigilance master file is two-fold: to concentrate information in one global document and to facilitate maintenance by uncoupling it from the marketing authorisation. Therefore changes to the content of the master file will no longer subject to variation obligations. Would it be nevertheless appropriate to require the marketing authorisation holder to notify significant changes/modifications to the master file to the competent authorities in order to facilitate supervision tasks? If so, how should this be done? Should the master file contain a date when it was last reviewed?

Marketing authorisation holders (MAHs) should not be required to notify changes to the pharmacovigilance system master file to the competent authorities. A formal process for defining and notifying such changes would result in an administrative burden on both the MAH and

Janssen Research & Development
50-100 Holmers Farm Way, High Wycombe
Buckinghamshire HP12 4DP, United Kingdom
Phone: +44 (0)1494 658000
Fax: +44 (0)1494 658001

Registered Office
Janssen-Cilag Ltd, 50-100 Holmers Farm Way
High Wycombe, Buckinghamshire HP12 4EG
Registered in England no: 1027904

competent authorities that is similar to that currently being experienced in relation to notification of changes to the Detailed Description of Pharmacovigilance System under the variations procedure.

The pharmacovigilance system master file will be version controlled, and as proposed in Section 5 of the concept paper, significant changes/modifications will be captured in a 'logbook' or history of changes table. As the national competent authority and European Medicines Agency (EMA) can request the MAH to submit a copy of the master file at any time, per Article 23 of Directive 2001/83/EC and Article 16 of Regulation (EC) No 1394/2007, this should be considered sufficient to facilitate supervision.

Consultation item no. 3: Is it necessary to be more precise on potential delegation, e.g. in the case of co-marketing of products? Please comment.

It would be helpful to clarify that delegation of tasks in this section refers only to those major contractual agreements whereby pharmacovigilance activities may be outsourced and that it does not, necessarily, include all co-licensing and co-marketing agreements. It is reasonable to require a description of major contractual agreements for outsourced pharmacovigilance activities to be included in the master file. However, the master file describes the pharmacovigilance systems 'uncoupled' from marketing authorisations (MAs), meaning that it is not product-specific. Therefore, for product-specific co-marketing / co-licensing arrangements it would be preferable to have a reference in the master file, in the form of a listing only, to the specific pharmacovigilance agreement in place for each applicable product.

With the complexities of the pharmaceutical industry, some companies will have a significant number of co-marketing and co-licensing arrangements. These are usually stored in a centralised and validated system and can be made available to the competent authority or EMA on request. With the current proposal, there will be a need to duplicate documentation already held in validated repositories, which is inappropriate and unnecessary. Contractual responsibilities change over time, which will introduce a potential risk of discrepancy between systems as well as additional administrative burden.

Consultation item no. 4: Should a copy of the audit report be retained in the master file? Would it be appropriate to require documentation of audit schedules?

A copy of the audit report should not be retained in the master file. A list of conducted audits should be sufficient evidence that there is an active and comprehensive audit program in place. An inspector may still request to see an audit report during inspection if they suspect that an adequate audit program was not in place. Additionally, companies have a computerised and

validated system that tracks audits. Again, it would be more efficient to reference the official controlled source of such information rather than duplicating it in the master file.

Consultation item no. 5: Overall, do you agree with the requirements as regards the content and maintenance of the pharmacovigilance master file? Please comment.

The pharmacovigilance system master file as currently proposed will be difficult to maintain in a global regulatory environment that is constantly evolving. We agree in principle with the need for one global document to describe key elements of a pharmacovigilance system; however, inclusion of other documents held in validated systems would be burdensome for companies to maintain, in addition to concerns of managing duplicate documents. A large company, such as Janssen, could potentially require a full time position in order to maintain a master file as currently outlined in this concept paper.

The types of documentation currently proposed to be included in the master file are usually held in centralised and validated tracking systems that are fit for purpose. In general, we are against duplicating such documentation in the master file, and recommend the master file cross-reference the original validated source for such information in each appropriate section. Copies of specific documentation (e.g. copies of contracts or procedures) from these systems may be made available by the MAH to the national competent authority and EMA if required. The master file would be more efficient to maintain in this format and the risk of discrepancies or inaccuracies between the master file contents and any validated tracking systems would be dramatically reduced.

The following are additional comments on specific items proposed within the pharmacovigilance system master file.

- With regard to the requirement to describe the quality system in the master file (*3. Content, point 7*), a reference should be made to the requirements described in Sections B and C of the concept paper (*Quality systems for the performance of pharmacovigilance activities*) to ensure consistency between what is described in the master file and required of MAHs in the way of a quality system. As currently written the relevant sections are inconsistent in places and difficult to follow. For example, under *11. Performance Indicators*, it states that "where indicators are used to continuously monitor the good performance of pharmacovigilance activities, those indicators and their results shall be documented. For MAHs, this shall be done in an annex to the pharmacovigilance system master file." However, no mention of this is made in Section A, which relates to the content and maintenance of the master file.
- With regard to the requirement to describe "the resource management of the performance of pharmacovigilance activities" (*3. Content, point 7b*), it is not clear what

"resource management" is meant to entail. It would be helpful to outline in the Good Vigilance Practice guide what types of activities or documentation should be included in this description.

- With reference to the requirement to maintain a logbook within the master file to track any alteration of its content within the past 5 years (*5. Documentation*), we would like to recommend that entries be limited to a defined set of significant changes/modifications relevant to pharmacovigilance activities conducted in the European Economic Area (EEA). With the volume of information required in the master file and as part of the continuous improvement processes of a pharmacovigilance system, there are likely to be an overwhelming number of individual updates and changes to procedures, contracts, and other elements described. This is particularly true for large pharmaceutical companies. Limiting logbook entries to those that are most significant and relevant would help facilitate maintenance of the overall document and still enable competent authorities to fulfil their supervision tasks.
- Regarding the requirement to place a note concerning the main findings of an audit in the master file (7. Audit), we support the proposal previously made by European Federation of Pharmaceutical Industries and Associations (EFPIA) to clarify 'main findings' as only those considered 'critical' or 'major' in nature.
- The second paragraph of *8. Inspection* states "The national competent authority and the EMA may at any time ask the MAH to submit a copy of the pharmacovigilance system master file." Please clarify whether "The national competent authority" refers to the competent authority of the member state where the pharmacovigilance system master file is located (i.e. the supervisory authority) or any national competent authority of any member state in the EEA where a local affiliate serves as MAH for medicinal products.
- The concept paper does not indicate which language the pharmacovigilance system master file should be written in. We feel that this is an important point, as translation of what may be a quite lengthy document may introduce delays in submitting the master file upon request. We would like to recommend the Commission stipulate that the pharmacovigilance system master file be written in English; and that translation of the master file shall not be required prior to submission to a national competent authority or the EMA.

B. Quality Systems for the performance of pharmacovigilance activities – Common obligations

C. Quality Systems for the performance of pharmacovigilance activities by marketing authorisation holders

Consultation item no. 6: Is there a need for additional quality procedures, e.g. in relation to study reporting in accordance with Article 107p of the Directive, in relation to communication on pharmacovigilance between the marketing authorisation holder and patients/health professionals; in relation to processes for taking corrective and improvement actions or in relation to the detection of duplicates of suspected adverse reaction reports in the EudraVigilance database?

Additional quality procedures are not needed in this implementing measure. However, the Good Vigilance Practice Guide should address the following in relation to quality system procedures already listed:

- Specific guidance on the criteria for correctness and completeness of all pharmacovigilance information required to be submitted to the competent authorities and EMA, especially regarding the processing of non-serious cases which may be processed differently (i.e. level of medical review) than serious cases
- In principle, we agree with the requirement for MAH to check the European medicines web-portal for any relevant updates. However, this should not replace formal and direct communication between the MAH and competent authorities regarding specific product information and safety issues. For safety measures or communications regarding a particular product we would still expect the competent authorities to notify the MAH directly prior to any information being posted on a public web-portal. Additionally, we would like to recommend the web-portal functionalities include an alert subscription service to facilitate notification to MAHs of new content added to the web-portal.
- Guidance on methods for detection of duplicate reports. In particular, more guidance is required on EMA's process for monitoring certain literature sources for reports related to specified medicinal products and how MAHs should monitor for such reports to avoid duplicate submission of literature cases which are EMA's responsibility.

Consultation item no. 7: Do you agree with the requirements for marketing authorisation holders? Please comment.

It is not clear which section of the concept paper this consultation item refers to. Assuming this consultation item refers to all content presented in Sections B and C we would like to make the following specific comments regarding these requirements:

- The requirement to perform quality system audits at regular intervals and not less than every two years can be interpreted very broadly (*10. Audit*). At one extreme an interpretation could be that only one audit of the whole system is mandated every 2 years. For a very small company at one location this may be sufficient, but for large

multinational companies a range of audits may be necessary to cover the size, complexity and geographic diversity of a global pharmacovigilance system. We would like to recommend the following change to this subsection: "Audits of the quality system shall be performed at ~~regular intervals, and not less than every two years,~~ to assure that the quality system is in compliance with the established quality system requirements and to determine its effectiveness. The frequency and number of audits should be based on a risk-based approach such that on average each aspect of the pharmacovigilance system would be audited every 3 years."

- Regarding the requirements under *13. Resource Management*, we would like to propose the second paragraph of this subsection be revised to read "duties of ~~the managerial and supervisory~~ all pharmacovigilance staff, including the qualified person for pharmacovigilance shall be defined in a job description". Per the third subparagraph of this subsection all personnel involved in the performance of pharmacovigilance activities shall receive initial and continued training. That training should be in relation to their role and responsibilities as outlined in a job description.
- Also regarding *13. Resource Management*, the fourth paragraph of this subsection indicates "Appropriate instructions on critical processes, including business continuity, shall be provided". Critical processes should be defined in the Good Vigilance Practice guide.

D. Quality systems for the performance of pharmacovigilance activities by national competent authorities and EMA

Consultation item no. 8: Do you agree with the quality system requirements? Please comment, if appropriate separately as regards for marketing authorisation holders, national authorities and EMA.

As a MAH, our comments on the quality system requirements are presented above in relation consultation item no. 7.With regards to quality system requirements for national competent authorities and the EMA, we feel it is important to stress that all competent authorities in the EU apply the same standards consistently and that this be captured in the requirements for quality systems. Variations in the standards applied to pharmacovigilance activities between national competent authorities causes significant administrative burden on industry and may divert resources from more valuable safety monitoring activities.

E. Signal detection and risk identification

Consultation item no. 9: For efficiency reasons a 'work sharing' procedure could be appropriate for the monitoring of medicinal products or active substances contained in several medical product. However, do you see a risk in cumulating all tasks (for the authorisation, PSUR scrutiny and EudraVigilance monitoring) in one Member State, as thereby the benefits of parallel monitoring may be lost ("peer review" system)? Additionally, it may be envisaged to extend 'work sharing' to all medicinal products (including all centrally approved products) and to appoint a lead Member State in addition to EMA (Article 28a(1)(c) of Regulation (EC) No 726/2004). Please comment.

We do not see a risk in cumulating all tasks in one Member State, as already occurs for centrally authorised products. We agree that it is appropriate extend 'work sharing' to all medicinal products and to appoint a lead member state to ensure resources are distributed efficiently. However, all tasks should not be assigned to one Member State without providing the other Member States an opportunity to comment, unless the product concerned was only authorised in one Member State.

Consultation item no. 10: In the Commission's view the aim of this part is to establish common triggers for signal detection; to clarify the respective monitoring roles of marketing authorisation holders, national competent authorities and EMA; and to identify how signals are picked up? Are the proposed provision sufficiently clear and transparent or should they be more detailed? If so, which aspects require additional considerations and what should be required? Please comment.

The language in this part does not adequately "establish common triggers for signal detection" on its own. More detail, including practical examples, regarding common triggers for identification of signal as defined in *21. Changed risks/new risks* should be provided in the Good Vigilance Practice guide. In particular, the role of single case review versus aggregate review should be addressed.

It is also unclear what is being required of the MAH in this part. Although the MAH is mentioned in subsections 20 and 23, specifically that the MAH "shall ensure continuous monitoring of the EudraVigilance database," the majority of this section seems to be directed toward EMA and those activities of the Pharmacovigilance Risk Assessment Committee. We would like to propose that the Commission address the roles of the MAH, national competent authorities and EMA individually in this section to clearly delineate the responsibilities of each for monitoring EudraVigilance in order to help each fulfil their respective obligations.

Additionally, the process for communication between the MAH, national competent authorities and EMA has not been addressed in this part. Article 107h(3) of Directive 2001/83/EC states "The Agency and national competent authorities and the MAH shall inform each other in the event of new risks or risks that have changed or changes to the risk-benefit balance being detected." A process for communicating the detection and evaluation of signals should be clarified. In particular, the process should indicate how the MAH may provide input or additional information into the evaluation of a signal detected through monitoring of the EudraVigilance database.

F. Use of terminology

Consultation item no. 11: Do you agree with the proposed terminology? Please comment.

We agree with the proposed terminology.

Consultation item no. 12: Do you agree with the list of internationally agreed formats and standards? Please comment.

We generally agree with formats and standards listed. However, while standards are a good starting point they are not sufficient on their own to enable industry to have a clear view of what actual information the EMA requires by 2 July 2012. A significant amount of effort will be required to take the standards and apply them to data and information that has been created prior to the approval of these standards. The EMA has yet to clearly define exactly what information they expect to be provided within the structures that they have published to date and how that relates to the various submission types from which much of the data will be extracted.

With this in mind, the deadline of 2 July 2012 for submission of data as currently described in the documents that EMA has released is very optimistic. Pharmaceutical companies will not only have to build and validate technology to enable the collection, submission and maintenance of the data once EMA provides a definitive statement of what they require, but they will have the additional challenge of mapping data that was created to meet different standards, much of it at a national level, into this new format.

G. Transmission and Submission requirements

Consultation item no. 13: Is there additionally a need for transitional provisions as regards certain aspects of this implementing measure, especially in relation to the specifications on format and content? Please comment.

In order to ensure legal certainty, the implementation measure must explicitly describe how transitional measures are to be put in place, particularly regarding periodic safety update reports (PSURs), risk management plans (RMPs) and post-authorisation safety studies (PASS), the details of which should be specified in the Good Vigilance Practice guide.

The following are our specific concerns regarding transitional measures for each area we have identified.

- Regarding *Subsection 30 Risk management plans*: In the absence of detail and clarity around the new requirements, immediate implementation of the new requirement for inclusion of plans for studies on effectiveness and long term efficacy is not feasible for authorised medicinal products with existing RMPs. Transitional measures should be considered with relation to the new RMP section "Part IV: Plans for studies on effectiveness and long term efficacy" for authorised medicinal products with existing RMPs, while mutually agreeable approaches are finalised between MAH and competent authority. Without such transitional requirements, the new implementing measures could in effect cause an immediate compliance issue for authorised medicinal products with existing RMPs. Marketing Authorisation Applications (MAAs) planned for submission shortly after July 2012 and those whose procedures are ongoing and due to end after July will also be at risk without detailed guidance to help companies ensure applications will be compliant with the new requirements.
- With regard to *Subsection 31 Periodic Safety Update Reports*: A transitional measure is needed for new aspects regarding routine PSUR reporting. In particular, there is a need for clarity regarding how products will be redefined as "low risk" or "high risk"; how the periodicity for products requiring routine reporting will be determined; how the reporting cut-off points for exempt products will be determined; as well as the procedure for communicating reporting requirements to MAHs including whether the MAH will have an opportunity to respond to these decisions. The Good Vigilance Practice guide should also clarify whether "low risk" products will require routine surveillance and submission of some other reports such as line listings or cumulative data.

  Transitional measures will need to be identified for PSUR date harmonisation and work-sharing. These measures should include a process for MAH input.

Additionally, a transitional measure is needed to clarify the submission of PSURs prior to implementation of the e-submission platform. This measure should facilitate transfer from the existing PSUR submission process to the centralised electronic PSUR repository submission method once implemented.

- Regarding Subsection *32 Post-authorisation Safety Studies*: In studies for which the protocol is already ongoing, and those studies for which contracts with investigators and independent research groups are already in place, it would not be practical to apply the new requirements. Transitional measures should be put in place for all post-authorisation studies that have already commenced. In addition, we recommend sufficient time be allowed for the implementation of these requirements for post-authorisation studies which are expected to start soon (e.g. within one year) after the publication of the final implementing measures. Without such transitional requirements, the new implementing measures could in effect cause a delay to the start-up of new post-authorisation studies.
- Additionally, with regards to ensuring that data on serious and non-serious reactions are submitted to the EudraVigilance database within the timelines stipulated by Article 107 in Directive 2001/83/EC (*14. Compliance Management, point b*) we wish to point out that submission of non-serious cases will be a big resource and system capacity requirement. Due to very large volumes of non-serious cases there will be an extra burden on EudraVigilance and gateway during the submission process. Therefore, capacity testing will be required to ensure non-serious submissions do not compromise compliance of serious case reporting and should be incorporated into a transitional measure for the new non-serious reporting requirements.

Annex I – Electronic submissions of suspected adverse reactions

Consultation item no. 14: Do you agree with the proposed format and content? Please comment.

We generally agree with the proposed format and content. However, under section 1 "Definitions" off label use should be clearly defined as distinct from misuse. Regarding this point we support the proposal made by EFPIA to revise the text of this section.

Additionally, the following clarifications of requirements in this annex should be provided in the Good Vigilance Practice guide:

- Paragraph 1(c): clarify with more detail what is considered "Above the maximal recommended dose." For example, if the patient one day takes one extra pill than instructed and there are studies that indicate the dose taken is safe for use, then many times it may not be considered overdose, however, there are interpretations that would consider any dose above the recommended dose instructed to the patient as "overdose" in the more strict sense of the definition.
- Paragraph 4(b): clarify what is meant by a 'comprehensive' English summary of the article;
- Paragraph 4(m): clarify whether or not a new report version should be transmitted in the event that no additional information has been secured via follow-up, and only to confirm "no further information available".
- Clarification of whether reports of abuse, misuse, medication errors, off label use without an AE should be submitted and the timeframe for submission.
- Additional guidance for management of "invalid cases" (i.e., cases that do not have all 4 minimum criteria).

Annex II – Risk management plans

Consultation item no. 15: Do you agree with the proposed format and content? Please comment.

We generally agree with the proposed format and content for RMPs as required in the legislation. However, it would be helpful to clarify if "Part IV. Plans for studies on effectiveness and long term efficacy" refers to only those studies mandated under revised Articles 9(4) and 10a(1) of Regulation (EC) No. 726/2004 and Articles 21a and 22a of Directive 2001/83/EC or if Part IV is meant to include all studies planned, even those outside the context of the MA in the EU.

Annex III – Electronic periodic safety update reports

Consultation item no. 16: Do you agree with the proposed format and content? Please comment.

In order to facilitate monitoring the safety of patients worldwide, PSURs are prepared and submitted on a global basis; therefore, it is important to maintain global harmonisation with regard to format and content of the report. We strongly recommend the Commission harmonise this implementing measure to the format and content being proposed in ICH E2C (R2).

With regard to the current proposal in this concept paper, the following specific requirements in this part should also be clarified and/or addressed:

- The proposed format is lengthy – a total of 20 proposed modules. Some of the proposed sections can be combined to read better and minimise the number of sections. For example, Sections 15, 16 and 17 could be integrated as could Sections 7, 8 and 9.

Section 13 may also be integrated into Section 7. However, we would like to again strongly encourage the Commission to adopt the proposed ICH E2C (R2) format currently being discussed.

- A back-up method for PSUR submission should be identified in the event that electronic submission to the centralised repository is unavailable. Details of a back-up method for PSUR submission once the PSUR repository has been implemented are necessary to ensure compliance if there are problems with electronic submission.
- The requirement for exposure estimation indicates "an accurate estimation of the population exposed to the medicinal product" should be provided. Please clarify whether it is the Commission's intention to require extra studies to be carried out in order to obtain data on actual use necessary to provide the analysis requested. Additionally the Good Vigilance Practice guide should provide more detail on the methodology/terminology that should be used to differentiate indicated versus actual use.

In addition to the requirements for electronic PSURs outlined in this Annex the following elements should also addressed in the Good Vigilance Practice guide:

- Directive 2001/83/EC clarifies that the focus of the PSURs should be to periodically evaluate risk-benefit balance of a medicinal product, based on all available data. It is as yet still unclear how benefit will be measured in post-marketed data to be address in the PSUR. The Good Vigilance Practice guide should establish specific and common post-marketing end-points to continually evaluate benefit and further detail on how evaluation of the benefit should be addressed within the context of the PSUR.
- Section 5.1 (Cumulative Subject Exposure in Clinical Trials): It is understood this will be the total number of clinical trial subjects over the life time of the development of the product. It may be particularly difficult to obtain this number for well established products that are not exempt for PSUR reporting requirements but which have significant global post marketing trials. Some flexibility should be introduced within the new template to account for such product-specific differences.
- Section 6.1 (Reference Information): Please clarify what is referred to in this section
- Section 6.2 (Cumulative Summary Tabulations of SAEs from Clinical Trials): This will have a big impact. Database upgrade will be required. Is there a case for combining the PSURs and DSURs into one report in future?

- Section 7.4 (Other Therapeutic Use of Investigational Drug): Please clarify the rationale for including this as a section in a PSUR. This seems to be more appropriate for a DSUR, rather than a PSUR. Inclusion of this could be something the EMA requests the MAH to include for a product for the initial X months/years of its lifecycle.
- Section 9 (Other Clinical Trial/Safety Information): Please clarify that this refers to other non-company sponsored clinical trial/study information. All company sponsored clinical trial information will be summarised in Section 7.
- Section 10 (Non-clinical Data): Please clarify the rationale for including this as a section in a PSUR. This seems to be more appropriate for a DSUR, rather than a PSUR. Inclusion of this could be something the EMA requests the MAH to include for a product for the initial X moths/years of its lifecycle.
- Section 12 (Other Periodic Reports): Please provide examples of "other periodic reports" during the interval reporting period of the PSUR.
- Section 16 (Signal and Risk Evaluation): Please clarify if the discussion on medical topics of interest will go into this section and whether this section will contain the information currently included in Section 9 of the PSUR (overdose, abuse, interactions, pregnancy, etc).
- Section 16 (Signal and Risk Evaluation): Please clarify whether it will be sufficient to either cross-reference the relevant risk management sections of the RMP or "copy and paste" necessary information from the RMP into this section of the PSUR.
- Section 20 (Region-specific Information): Please clarify the type of detail required in this section including a definition of the regions to be discussed. Furthermore, clarification regarding whether this should be population specific information regarding a specific region i.e. pharmacoepidemiology or a high level case overview would be useful.

Annex IV – Protocols, abstracts and final study reports for the post-authorisation safety studies

Consultation item no. 17: Do you agree with the proposed format? Please comment.

The following specific points in this annex should be clarified:

Scope and Definitions

Point 1 indicates that PASS financed by a MAH, pursuant to obligations imposed by a national competent authority or EMA, are within scope the requirements outlined in this annex. However, in many cases, such studies are only partially financed by one MAH, only a specific analysis/dataset is acquired from an independent research group or the MAH begins participating

in an independent study already underway. In such cases, where the MAH is only one of the stakeholders involved in a study, the protocol is not owned by the MAH. The current proposals seem strongly focused on such studies where the MAH is the sole owner of a post-authorisation study, which is often not the case. The current proposal should be modified to adequately address such situations where these studies are only partially financed by the MAH.

In point 1.6, clear timelines should also be established for submission of amendments to protocols.

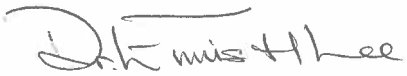
Format of the study protocol

Regarding point *2.13 Resources required to conduct the study*, there should be no reason to report on resources need. Studies will be conducted in accordance with GCP and therefore adequate resources will be guaranteed by way of such conduct. There should be no need to outline this specifically in a protocol.

Format of the abstract of the final study report

Only the final study report is described in this annex. However, in current practice, annual or bi-annual reports of safety studies are commonly required. It would be helpful if the Good Vigilance Practice guide clarified whether format for final study reports should also be enforced upon such (interim) reports.

Yours faithfully,



Dr. Ennis H. Lee
Vice President, EEA QPPV Pharma
Janssen Pharmaceutical Companies of Johnson & Johnson

Cc: A. Papin
K. Van Baelen
Y. Yap