SUBMISSION OF COMMENTS ON <GUIDELINE TITLE> <DOCUMENT REFERENCE>

COMMENTS FROM <ORGANISATION / CONTACT PERSON>
GENERAL COMMENTS
In general, the majority of changes proposed within this draft legislation are well thought through and very much welcomed. The comments below focus on our major areas of concern e.g. items of significant practical/logistical impact, areas where compliance questions arise, and areas for which clarification is requested.
We note that the target for a new Directive and Regulation is 4Q 2008. Will industry have opportunity to comment again or is this our only opportunity?

SPECIFIC COMMENTS ON TEXT

GUIDELINE SECTION TITLE

Line no[1]. + paragraph no.	**Comment and Rationale**	**Proposed change (if applicable)**
3.2.1. Page 3 Paragraph 1	We are supportive of a stronger legal mandate of the PhVWP as a new committee coordinating pharmacovigilance and making safety recommendations. That said, we note that this section refers to this committee making recommendations to the CHMP, whereas the draft revision to Regulation Article 56(1)(aa) states the new Committee of Pharmacovigilance will have the status of a Committee under the EMEA equal to that of the CHMP and CVMP. How will this operate in practise?	Clarification of practical aspects of the new Committee requested i.e. - What will be the decision making process and will such decisions no longer need to be ratified by the CHMP? - What will fall within the scope of this new Committee? e.g. RMP reviews, signal detection, risk-benefit analysis etc.
3:2:1 Page 3/4	We welcome the concept of restriction of referrals for national products, and new "light" procedures and public hearings from a committee whose decisions will be implemented across the EU. That said, the term 'light oversight' or 'light procedures' is very vague, and the process around a public hearing is not fully defined.	Further clarification requested from the Commission with respect to the intent/definition of the terms 'light oversight' or 'light procedures. Further clarification also requested on what the triggers are for a public hearing, are they restricted to those mentioned in Chapter 6, Article 101k, 1; a to e? (Page 29) and does this article only apply to national and Mutual recognition or also Central products? Chapter 6, Article 101k, 6; states the agency shall notify of a public hearing within two working days via the web portal to both the public and the MAH. In this respect we suggest notification to the MAH in advance of release via

[1] Where available

		the web site to the public
3.2.2 Page 4	Noting that a further Regulation on Good Vigilance Practices will follow, GVP should be aligned with international standards per ICH E2D. Will this be the case?	Clarification requested if proposed Regulation on Good Vigilance Practices will be aligned with ICH E2D.
3.2.3 Page 5 And Pages 32 and 43	Fully support the concept of simplified detailed description of the PV system and the concept of PV system master file to be submitted on request or reviewed at inspection. Do not agree that the specific supervisory authority for PV for centrally authorised products should be the member state where the QP resides. The supervisory authority should be tied to the system, not to an individual, recognizing that the electronic age enables 'residence' criteria to be flexible for individuals. The provision as it currently stands could present issues for industry when hiring QPs, particularly for small MAHs who outsource the QPPV role as they would need to insist that the QPPPV be located at one EU country for inspection reasons. Tying inspections to the QP location may also exclude people from becoming QPs when residing in the smaller/newer member states.	The specific supervisory authority for PV should not be tied to the residence of the QPPV but should instead be assigned to a member state that the MAH designates as the most appropriate to support scrutiny of the PV system. This would normally be 'head office' state for EEA based companies, or may be the member state where the PV master file and system is housed/accessible in the EEA for MAHs with their HQ located outside the EEA, and/or where PV functions are split between different locations.
3.2.4 Page 5	Clear examples should be provided of when risk management plans are "needed" otherwise the authorization process may be delayed. Care must be given to the interpretation of "compliance" to RMP commitments, as in some cases every effort can be made to conduct a safety study but circumstances unforeseen by the MAH or authorities may make it impossible, for instance, to recruit within agreed timelines.	Introduce text to indicate that focus should be on special commitments related to true Public Health issues with scientific justification, and that any requests for such commitments must be both practical and achievable. Companies should be deemed in compliance if they can prove that all reasonable efforts were made to conduct the RMP obligations.
3.2.5 Page 6 And Article 101g/h Page 26/27	We welcome efforts to harmonize national legislation in regard to Post Authorization safety studies but there does need to be more clarity around the definition of PASS studies in line with the EFPIA PASS position paper In addition, what does "light oversight mean" in this section, and what is the value added if protocols are reviewed and progress reports are written? We have practical concerns about PASS studies requested by agents other than the CAs, such as pricing authorities, or conducted by external agents such as Physicians and Academic Institutions. Industry is usually obligated to provide some support/sponsorship to such studies but often has little control or access to data to enable	We propose that consideration be given to the contents of the EFPIA 2007 position paper on PAS/PASS With respect to PASS studies requested by agents other than the CAs, we request that such circumstances are acknowledged in the legislation as currently only one source of initiation/conduct of such studies is recognized, i.e. those of the MAHs.

	the new provisions around such studies outlined in Article 101h to be adhered to.	
3.2.6 Page 7 And Page 23, Article101e	We welcome that all serious 3rd country reports go to Eudravigilance only, noting that it is essential that individual MS CAs will commit to removing any local requirement to also submit directly to them as this would defeat the object of the proposal. With respect to the above, and to the second bullet which requires "all EU domestic reports only to go to Eudravigilance", it is a major change for all ICSRs to be required within 15 days (regardless of seriousness and/or expectedness). If this is to be the case it will present a huge logistical problem to industry in terms of prioritising workload, plus presumably Agencies will need to provide industry with both SAES and NSAES sent directly to them within the same timeframes. It will be important to ensure that individual countries do not have in addition to the EU list of compounds under intensive monitoring their own country lists of additional compounds under intensive monitoring as is the case at present.	Suggest that, all reports not being equal, timeframes for reporting continue to reflect the seriousness of the ICSR in question. Lists of products under intensive monitoring should be maintained at the EU rather than the MS level.
3.2.6 Page 7	We disagree that each pack should contain an adverse reaction reporting form as this will make current packs much bigger and interfere with manufacturing operations, particularly given multiple language requirements within the EEA. We would suggest that this AE reporting form is distributed for products under intensive monitoring by pharmacists and physicians. It may be confusing for patients to be asked to report to the MAH for intensively monitored drugs if there are also routes in place for reporting to the National Agency (as already exist in some MSs). Suggest that both reporting routes should be acceptable with MAH and CA having access to the data in Eudravigilance.	Suggest that the AE reporting form is distributed for products under intensive monitoring by pharmacists and physicians.
3.2.7 Page 8	Although discontinuation of PSURs for old products would reduce workload, there would need to be consideration of matters such as when they need be re-initiated, a definition of what constitutes an "old product", the label change process in their absence, etc.	Consider introducing the original concept of a very much 'simplified' PSUR for older products combined with continued use of the recently introduced EU work-share process
3.2.8 Page 9 And 101i	We welcome the increased coordination of provision of safety information, but are concerned that significant differences in content of information could still exist between member states as the text makes it clear that EMEA will coordinate but not replace member	Suggest adding that there is one single contact point identified for the MAH for each product to report any safety issues. This could either be the EMEA, the Rapporteur or RMS or assigned PhVWP representative. The notification of the Regulator's Network would then be made along the same

Page 27	state communication How will the EMEA ensure standards with 27 MS websites?	communication lines as for all other safety alerts.
3.2.8 Page 8	The EU drug dictionary should drive to international standards under development.	Add reference to the International Standard under development (ICH M5)
3.2.9 Page 9	The key safety information section in the SPC in section 3 seems to be in a strange location. This section comes before the actual indication and it would give a wrong perception of the product. Benefits of the product should also be considered and not only risks. Results of large outcomes trials confirming providing further benefits to patients should be included in the indication section.	We would like to have a better understanding of the content of the new key safety section to be in a position to judge if this section provides added value or if another existing section could be revised to meet the needs. Suggest review of what is being done in US. Is this a transatlantic simplification opportunity?
Article 54 Page 18/19	With respect to additional wording on outer box and PIL for intensively monitored products, we suggest to use a pictogram or symbol to convey the message to patients and physicians due to limited space on outer cartons. As a fall back position we encourage the use of lay friendly term like "side effects" instead of "serious adverse reactions". Such phrase should also be used in the PIL to make this understandable to patients. We also suggest that a toll-free number or an e-mail address for reports to the MAH is included in the PIL instead of the full address.	
Article 59 (1) Page 19	Box with black border could be confusing as compared with Black Box warnings in US labels. Further clarity is required on "key safety information" and "how to minimize risks" – is this foreseen as being a mixture of dosing instructions, contraindications and primary side effects?	Is this another opportunity for transatlantic simplification?
Article 101e Page 23	The current text refers to all reports being *collated* at one point within the community, however this is not currently the case and highly impractical for non EU head office companies.	Suggest changing the word '*collated*' to '*accessible*' at one point in the community.
Article 101f Page 24	States that PSURs shall contain *'*all data' related to the volume of sales. This is very broad and not always practical. Should be clarified as 'relevant data' such that not every PSUR need have data broken down by region, country, age, dose etc.	Suggest change to 'all *relevant* data'
Article 101f Page 25	The review process for PSURs should be modelled on the current process available for CP products, which allows adequate time for discussion and interactions between the MAH and Regulators. http://www.emea.europa.eu/htms/human/postguidance/q78.htm	

	We would support that conclusions of PSUR assessments and recommendations for changes of product information are published, provided that this is done in lay language adapted to the audience. Such communications should be made available to the applicable MAH when posted. The recommendations would then be implemented in the MA via a minor variation (Type IA immediate change according to the new Variation regulation proposal).	
Article 101i 1f Page 28	There is absolutely no clear benefit to public health and transparency in making lists of QPs and the countries they live available, plus there are strong and serious privacy and personal safety concerns around this proposal (related to animal rights activists, patient activists etc.).	QP data should definitely not be made publicly available. A published contact number at the MAH for safety information plus the QPPV details being provided on a confidential basis to the CAs and The Agency (as now) should suffice.
Article 101i, 5 & 6 Page 28	The EMEA and PV Committee should drive the risk management plan communication to ensure consistency on MS Agency websites and also for products under intensive monitoring.	'All reasonable efforts' to agree common safety messages does not go far enough, common safety messages should be agreed by all member states
Article 101j Page 29	The purpose and intent of the "list of products under intensive monitoring" should clearly be communicated to the public. This should be an EU rather than per MS list. A mechanism to request a deletion from this list should be provided.	
Article 101l 4d Page 33	Signal detection in EV may in many non EU based companies be performed by individuals not located in the EU, thus EV access will need to be provided to expert individuals who may reside outside the EEA as delegated by the EU QPPV.	The wording in this paragraph must be changed to allow delegation of the list of the activities by the EUQPPV (even outside EEA)
Article 57(2) Page 44	The trial data fields should follow international WHO standards. The results database should look to clintrials.gov for opportunities to synchronize.	
Throughout	Suggest common terminology applied throughout e.g. risk management plan Vs risk management system, standardise references to the MAH (use 'they' rather than 'he') etc.	

Please feel free to add more rows if needed.