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PGEU Comments

STRATEGY TO BETTER PROTECT PUBLIC HEALTH BY STRENGTHENING AND RATIONALISING EU PHARMACOVIGILANCE

PGEU GPUE Groupement Pharmaceutique de l'Union Européenne
Pharmaceutical Group of the European Union

Rue du Luxembourg 19-21 ● B -1000 Brussels
Tel : +32 2 238 08 18 ● Fax +32 2 238 08 19
pharmacy@pgeu.eu ● www.pgeu.eu

1. Introduction

The Pharmaceutical Group of the European Union (PGEU) is the European association representing community pharmacists in 30 European countries including EU Member States, EEA countries and EU applicant countries. Within the enlarged EU, over 400.000 community pharmacists provide services throughout a network of more than 160.000 pharmacies, to an estimated 46 million European citizens daily.

PGEU's objective is to promote the role of pharmacists as key players in healthcare systems throughout Europe and to ensure that the views of the pharmacy profession are taken into account in the EU decision-making process.

PGEU welcomes the Commission's initiative to strengthening the pharmacovigilance system in the EU towards a higher level of protection of public health and the opportunity to present comments to the legislative proposals.

We strongly favour all efforts towards a robust and user friendly Pharmacovigilance system. To link the decision-making process of authorising a medicinal product to the robustness of the post-authorisation pharmacovigilance is an innovative approach that reflects advances in technology and EU coordination but needs a thorough analysis. It must not be kept out of sight that the key objective and priority should continue to be to protect public health, ensure patient safety and respond to patients' needs. Therefore the removal of any delays in authorising a new medicine must not jeopardise the current safety standards. Patients and healthcare professionals should be reassured that simplified procedures will not involve any additional risk to the patient and that authorised medicines continue to have a high safety profile. In our opinion, some of the simplifications proposed may be too ambitious and certainty that there will not be extra risks involved is not guaranteed. In addition and notwithstanding the fact that the proposed changes focus particularly on new medicines we are concerned with the proposed relaxation of the current rules for safety monitoring of those medicines which are on the market for a longer time. With this in mind, PGEU comments to the proposed changes will highlight those areas where we feel the proposed changes may have gone beyond the needed safety net. We will of course underline as well those aspects where we feel improvement would be achieved with the proposed changes.

As we have pointed out in previous consultations, we would like to underline the fact that it is extremely important to provide documents for consultation in all official EU languages in order to facilitate as broad a consultation process as possible.

2. Section 3 Legislative strategy and the key proposals for legislative change

Fast robust EU decision-making on safety issues by rationalising the existing EU referral procedures and reinforcing the committee structure

PGEU supports the establishment of a Pharmacovigilance Committee within the EMEA structure, to replace the existing Pharmacovigilance Working Party, as this would represent the reinforcement of coordination with regards to EMEA overall activity in the Pharmacovigilance domain and particularly in the development of recommendations on the safety of medicines. These can be implemented comprehensively across all Member States, therefore leading to convergent safety action by the Member States.

Overall, PGEU supports the simplification of procedures as long as these will ensure that pharmaceutical companies and competent authorities will fully comply with safety requirements. We cannot accept that simplification is done solely on the basis of saving costs and to remove the administrative burden, if that will lead to lower quality standards of procedures. We are glad to acknowledge that the proposed changes seem to have covered this concern and we therefore

welcome the creation of the automatic pharmacovigilance referral. Nonetheless, it will be critical to ensure that the automatic notification reach, at the same time, other Member States, the Agency and the Commission. We expect that the practical application of the automatic pharmacovigilance referral will lead to a process where when a Member State reports an incident this is notified simultaneously to other Member States, the Agency and the Commission.

In relation to the proposed Article 101k, an in particular with regards to ***temporary suspensions***, we would like to point out the importance of complying with maximum time limits to notify competent authorities in those Member States where the medicinal product in question is also marketed. It would be important to ensure that these notifications are carried out without delay, for example by stating exact dates and short time limits.

Clarify/codify roles and responsibilities and codify standards for industry and regulators

As it has been appropriately highlighted in the consultation background paper, those directly involved in pharmacovigilance include: patients as the users of medicines; doctors, pharmacists, nurses and all other healthcare professionals working with medicines; regulatory authorities including the European Medicines Agency and those in each Member State responsible for monitoring the safety of medicines; pharmaceutical companies, and companies importing or distributing medicines. We would therefore expect that ***roles and responsibilities for all these agents should be taken into consideration***.

PGEU welcomes the clarification of roles and responsibilities for industry and regulators, however we are particularly concerned by the lack of a reference to the role of health professionals in the proposed legislation changes.

When safety of medicines is questioned, in practice and real life, health professionals such as doctors, pharmacists, and nurses will be the first ones to be addressed by the general public. As healthcare systems gatekeepers, they can ensure that unsafe medicines are not distributed as well as inform patients about possible increased risks they might be facing when taking certain medicines. Moreover in case of withdrawal of products from the market community pharmacists are the key health professionals who will ensure that in collaboration with wholesalers and pharmaceutical companies, a smooth, quick and effective removal of products from the market will be achieved. They will also be the ones most exposed and most likely to be addressed by the general public regarding safety concerns. Therefore, we believe that such role should be included in the legislative proposal.

It is important to note that pharmacists' role in monitoring medicinal products is not confined to reporting adverse drug reactions and other drug-related problems. It also involves monitoring the introduction of generic or therapeutically equivalent medicines and reviewing older medicines, traditional, complementary and alternative medicines, non-prescription medicines, blood products, biologicals, medical devices and vaccines[1], while providing at the same time all relevant information to individual patients with regards to benefits and risks associated with the use of these medicines and medical devices.

Additionally important is the fact that pharmacists come into contact with groups of patients that for ethical and/or practical reasons are not routinely involved in clinical trials, (e.g. pregnant women, children, elderly people and people using many drugs simultaneously). This is also an argument which could justify further involvement of pharmacists as a resource for phase IV clinical trials.

PGEU had already highlighted this aspect in its submission to the Commission consultation "An assessment of the Community System of Pharmacovigilance" in May 2006. However this seems not to have been given sufficient relevance in the proposals for legislative changes.

[1] FIP Statement of Policy "The Role of the Pharmacists in Pharmacovigilance", August 2006

In our opinion, to reduce the reference to health professionals to the sole aspect of encouraging them to report suspect adverse reactions (Article 101a) falls short in recognising their importance and clarifying their responsibility in improving the pharmacovigilance system. The particular aspect of communication between healthcare professionals, patients and the public in general is completely unmentioned and is without doubt a critical factor to enhancing the pharmacovigilance system.

Healthcare professional organisations play a relevant role in improving professional practice and can collaborate with competent authorities in the implementation of policies and measures to enhance healthcare professionals' contribution to the pharmacovigilance system.

Therefore we would suggest the following additions:

Commission Proposal	**Suggested text by PGEU**
Article 101b(1)	**Article 101b(1)**
Following consultation with the Agency, Member States and interested parties, and in accordance with the procedure referred to in Article 121 (2), the Commission may adopt guidelines on good pharmacovigilance practice including technical rules and procedures for: **(…)** ➢ Scientific and procedural guidelines on audit by the Marketing Authorisation Holders, National Competent Authorities and Agency of their performance of pharmacovigilance.	Following consultation with the Agency, Member States and interested parties ***(including health care professionals' representatives)***, and in accordance with the procedure referred to in Article 121 (2), the Commission may adopt guidelines on good pharmacovigilance practice including technical rules and procedures for: **(…)** ➢ Scientific and procedural guidelines on audit by the Marketing Authorisation Holders, National Competent Authorities, ***healthcare professional organisations*** and Agency of their performance of pharmacovigilance.
Article 101b(2)	**Article 101b(2)**
Marketing authorisation holders, the Agency and the competent authorities shall follow the guidelines referred to in paragraph 1 in the fulfilment of their tasks related to pharmacovigilance.	Marketing authorisation holders, the Agency, the competent authorities ***and the healthcare professional organisations*** shall follow the guidelines referred to in paragraph 1 in the fulfilment of their tasks related to pharmacovigilance.
Article 101d(2)	**Article 101d(2)**
The Agency, in collaboration with the Member State Competent Authorities, shall monitor the data in Eudravigilance for signals of new or changing risks of medicinal products authorised in the Community. In the event of a change being detected the Agency shall inform the marketing authorisation holder, the Member States and the Commission of these findings.	The Agency, in collaboration with the Member State Competent Authorities, shall monitor the data in Eudravigilance for signals of new or changing risks of medicinal products authorised in the Community. In the event of a change being detected the Agency shall inform the marketing authorisation holder, the Member States ***(including competent authorities and healthcare professional organisations)*** and the Commission of these findings.
Article 101l(2)	**Article 101l(2)**
In addition to the general responsibilities as competent and supervisory authority and the specific responsibilities and tasks laid down in Articles 101a to 101k above, the Member States shall: a) Designate a competent authority for the conduct of pharmacovigilance. b) Designate a supervisory authority for pharmacovigilance inspections. c) If the qualified person for pharmacovigilance for a centrally authorised product resides in that Member State then the Member State shall act as the	In addition to the general responsibilities as competent and supervisory authority and the specific responsibilities and tasks laid down in Articles 101a to 101k above, the Member States shall: a) Designate a competent authority for the conduct of pharmacovigilance. b) Designate a supervisory authority for pharmacovigilance inspections. c) If the qualified person for pharmacovigilance for a centrally authorised product resides in that Member State then the Member State shall act as the

supervisory authority for pharmacovigilance inspections. d) Operate a pharmacovigilance system to collect information useful in the surveillance of medicinal products, with particular reference to adverse reactions in human beings and evaluating such information scientifically. The system shall have the ability to identify the medicinal products prescribed and dispensed which are the subjects of an adverse reaction report. e) Monitor data in Eudravigilance for signals of new or changing risks and for changes to the risk benefit balance o f medicinal products for which it is the competent authority and where no reference member state exis ts. f) In collaboration with the marketing authorisation holders, monitor the outcome of risk minimization measures relating to nationally authorized products. g) Upon the request of the Commission and under the coordination of the Agency, participate in international harmonization and standardization of technical measures in pharmacovigilance. h) Perform regular audit of its pharmacovigilance tasks including its performance of Good Vigilance Practices and report the results to the European Commission no later than -/- (two-years after the entry into force of this directive) and then yearly thereafter.	supervisory authority for pharmacovigilance inspections. d) Operate a pharmacovigilance system to collect information useful in the surveillance of medicinal products, with particular reference to adverse reactions in human beings and evaluating such information scientifically. The system shall have the ability to identify the medicinal products prescribed and dispensed which are the subjects of an adverse reaction report. e) Monitor data in Eudravigilance for signals of new or changing risks and for changes to the risk benefit balance o f medicinal products for which it is the competent authority and where no reference member state exists. ***f) In collaboration with healthcare professional organisations, identify national strategies for better involving healthcare professionals in the pharmacovigilance system*** ***g)*** In collaboration with the marketing authorisation holders, monitor the outcome of risk minimization measures relating to nationally authorized products. ***h)*** Upon the request of the Commission and under the coordination of the Agency, participate in international harmonization and standardization of technical measures in pharmacovigilance. ***i)*** Perform regular audit of its pharmacovigilance tasks including its performance of Good Vigilance Practices and report the results to the European Commission no later than -/- (two-years after the entry into force of this directive) and then yearly thereafter.

In connection with the above comment, we will address later in this submission the importance of feeding in the information systems available to health professionals as well as providing information tools easily accessible to health professionals.

Simplify informing the authorities about the company pharmacovigilance system

In contrast to what we mentioned before in relation to the automatic pharmacovigilance referral, where we favoured simplification, we are not so certain that this specific simplification will indeed ensure public health protection overall. The danger in simplifying the existing requirements for a 'detailed description of the pharmacovigilance system' lays in the fact that products, when entering the market will not be strictly monitored (only by request) and that industry might take this as a chance to postpone the development of their pharmacovigilance systems. In fact, a post-authorisation process relaying very much on the number and quality of inspections may not be satisfactory.

The proposed Article 8 (3)(ia) mentions that the applicant should include in the application for marketing authorisation a "reference to the site of the Pharmacovigilance system Master File for the medicinal products". Furthermore, in the proposed Article 23 it is preview the possibility for the competent authority to ask at any time "the holder of the marketing authorisation to submit a copy of the pharmacovigilance system master file". It is not clear for us how the competent authority or the Agency will analyse, if at all, the pharmacovigilance system master file within the process of evaluating the marketing authorisation.

Rationalise risk management planning

PGEU welcomes and strongly supports the changes envisaging clarifications and enforcement in relation to 'risk management systems'. This was indeed needed to ensure safety evaluation of products after they enter the market and are exposed to the wider population and particularly to certain population groups (e.g. children, elderly, pregnant women) not addressed in clinical trials.

We welcome the proposed inserting in article 21(1) that states that "the risk management system shall be annexed to the marketing authorisation".

The main goal of a RMS is to ensure that companies will have the necessary measures in place to minimise risk and preferably avoid it. It will be therefore of extreme importance that competent authorities and the Agency regularly audit the quality and the implementation of RMS.

In our opinion the RMS should not neglect the importance of collaborating with healthcare professionals in order to best communicate benefits and risks of medicines

With regards to the establishment of a European list of medicines under intensive monitoring (proposed change to Article 22), PGEU has some reservations on how effective this measure could be. We do not dispute the fact that establishing such a list could facilitate bringing new medicines more rapidly to the market, but we are concerned about their possible lower safety profile and undiscovered risks. Moreover, we are concerned by the fact that the proposed amendment to article 22 suggests deleting the notion of "exceptional circumstances" as well as the conditions that "the authorisation may be granted only for objective, verifiable reasons" and that the "continuation of the authorisation shall be linked to the annual reassessment of these conditions". The amendment may reflect the intention of granting authorisations following the conditions included in the proposed amended article 22 more often than exceptionally. In our opinion this should be taken carefully as there must be certainty that removal of delays does not involve any degree of extra risk for the patient.

Commission Proposal	**Suggested text by PGEU**
Article 22	**Article 22**
1. ~~In exceptional circumstances and following consultation with the applicant, the authorisation~~ A marketing authorisation may be granted subject to the following conditions, included in the risk management system: ~~may be granted subject to a requirement for the applicant to meet certain conditions, in particular: concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. This authorisation may be granted only for objective, verifiable reasons and must be based on one of the grounds set out in Annex I. Continuation of the authorisation shall be linked to the annual reassessment of these conditions. The list of these conditions shall be made publicly accessible without delay, together with deadlines and dates of fulfilment.~~ (a) the requirement to conduct post-authorisation safety studies, or, (b) adverse reaction recording or reporting that differs from the requirements of Title IX, or, (c) any conditions or restrictions with regard to the safe and effective use of the medicinal product. The marketing authorisation shall lay down deadlines for the fulfilment of the conditions where necessary. Continuation of the authorisation shall be linked to the fulfilment of these conditions and the assessment of any data resulting from the implementation of the conditions.	1. ***In exceptional circumstances*** ~~and following consultation with the applicant, the authorisation~~ a marketing authorisation may be granted subject to the following conditions, included in the risk management system: ~~may be granted subject to a requirement for the applicant to meet certain conditions, in particular: concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. This authorisation may be granted only for objective, verifiable reasons and must be based on one of the grounds set out in Annex I. Continuation of the authorisation shall be linked to the annual reassessment of these conditions. The list of these conditions shall be made publicly accessible without delay, together with deadlines and dates of fulfilment.~~ (a) the requirement to conduct post-authorisation safety studies, or, (b) adverse reaction recording or reporting that differs from the requirements of Title IX, or, (c) any conditions or restrictions with regard to the safe and effective use of the medicinal product. The marketing authorisation shall lay down deadlines for the fulfilment of the conditions where necessary. Continuation of the authorisation shall be linked to the fulfilment of these conditions and the ***annual*** assessment of any data resulting from the implementation of the conditions.

2. The Member States shall notify to the Agency the granting of marketing authorisations subject to conditions as referred to in paragraph 1 and these medicinal products shall be included in the European list of intensively monitored products referred to in Article 101j. A medicinal product shall be removed from the list when the competent authority which granted the marketing authorisation concludes that the measures referred to in paragraph 1 have been completed and that, following the assessment of any data resulting from the implementation of the conditions, the benefit -risk balance remains positive.	2. The Member States shall notify to the Agency the granting of marketing authorisations subject to conditions as referred to in paragraph 1 and these medicinal products shall be included in the European list of intensively monitored products referred to in Article 101j. A medicinal product shall be removed from the list when the competent authority which granted the marketing authorisation concludes that the measures referred to in paragraph 1 have been completed and that, following the assessment of any data resulting from the implementation of the conditions, the benefit -risk balance remains positive.

Codify oversight of non-interventional safety studies

PGEU welcomes this incentive for post-authorisation safety studies as we consider it will strengthen medicine safety and provide extensive and accurate measure after a product is authorised.

Simplify and make proportional reporting of single serious adverse drug reaction (ADR) case reports

PGEU believes that it is important to provide access to a user friendly Eudravigilance database, considering that not only experts on regulatory affairs but also health professionals in general and patients could make a better use of it. In this regard, we particularly welcome Article 101e (4), envisaging a "web-based structured reporting form for European healthcare professionals and patients to facilitate electronic reporting of ADRs and submission to Eudravigilance". For this purpose, we would like to underline the importance of involving not only the future Committee on Pharmacovigilance but also the patients and consumers' working party and the healthcare professionals' working group of EMEA. In addition to making available such reporting tool, it will be important that European healthcare professionals are aware of this tool and trained on how to use it. Therefore, incentives for healthcare professionals' continuous professional development could include this objective.

We believe that the database could be enhanced in order to allow the identification and reporting of what could be classified as minor ADR in the pharmacovigilance system but that still affect patients' quality of life (e.g. loss of appetite, insomnia, nightmares, hair loss, pain, etc).

In our opinion, all EU domestic reports should be addressed not only to the Member State where they occurred but also to all Member States. Moreover, warnings from other non-European markets regarding safety of medicines should be closely monitored, in order to ensure early detection of safety problems.

We welcome the reference in the proposed new article 101a that "member states shall take all appropriate measures to encourage doctors and other health care professionals to report suspected adverse reactions to the marketing authorisation holder or the competent authorities". We understand the general statement, but we would favour at least the identification of some possible ways of encouragement such as incentives to CPD, simplification of electronic reporting tools and their integration in existing computer systems at the point of the health professional practice.

Furthermore, and ***taking into account what we have already mentioned with regards to the pharmacist role in pharmacovigilance, we believe "pharmacists" as it is the case for doctors, should be clearly stated in the legislative proposal rather than included in "other health care professionals".***

Commission Proposal	Suggested text by PGEU
Article 101a	**Article 101a**
The Member States shall take all appropriate measures to encourage doctors and other health care professionals to report suspected adverse reactions to the marketing authorisation holder or the competent authorities. The Member States may impose specific requirements on doctors and other health-care professionals in respect of the reporting of suspected serious or unexpected adverse reactions. Through the methods of collecting information and where necessary through the follow up of adverse reaction reports, the Member States shall ensure that any biological medicinal product prescribed and dispensed in their territory which is the subject of an adverse reaction report is identifiable.	The Member States shall take all appropriate measures to encourage doctors, ***pharmacists*** and other health care professionals to report suspected adverse reactions to the marketing authorisation holder or the competent authorities. ***These could include, e.g., incentives for continuous professional development, simplification of electronic reporting tools and their integration in existing computer systems at the point of the health care professional practice.*** The Member States may impose specific requirements on doctors, ***pharmacists*** and other health-care professionals in respect of the reporting of suspected serious or unexpected adverse reactions. Through the methods of collecting information and where necessary through the follow up of adverse reaction reports, the Member States shall ensure that any biological medicinal product prescribed and dispensed in their territory which is the subject of an adverse reaction report is identifiable.

PGEU notes and welcomes the possibility for patients to self report adverse drug events. It is not clear, however, how information reported by patients in relation to intensively monitored medicines directly to the marketing authorisation holder only will then be integrated in the EU pharmacovigilance system in a transparent and timely manner. As far as we can see, the self reporting seems to be proposed only via the marketing authorisation holder. Has the possibility for self reporting by patients to the competent authorities been excluded? In our opinion, ***self reporting should not be misunderstood by direct reporting to the pharmaceutical industry and therefore not limited to this sole possibility***.

In any case, ***reporting should be complemented with a discussion between the patient who suffered an adverse reaction and his/her healthcare professional to ensure that benefits and risks are clearly identified and an alternative treatment solution may be found***.

Commission Proposal	Suggested text by PGEU
Article 11(3b)	**Article 11(3b)**
The summary of the product characteristics shall contain, in the order indicated below, the following information: (…) 3b. key safety information about the medicinal product and how to minimise risks. For medicinal products included on the European list of intensively monitored products referred to in Article 101j this information shall also include the statement "This medicinal product is under intensive monitoring. All suspected adverse reactions should be reported".	The summary of the product characteristics shall contain, in the order indicated below, the following information: (…) 3b. key safety information about the medicinal product and how to minimise risks. For medicinal products included on the European list of intensively monitored products referred to in Article 101j this information shall also include the statement "This medicinal product is under intensive monitoring. All suspected adverse reactions should be reported ***and discussed between the patient and his/her healthcare professional***".

According to the proposed Article 101e(1), all adverse reactions which have been brought to the attention of the marketing authorisation holder shall be recorded, but only those which the marketing authorisation holder self-evaluates as to be a reasonable possibility of causal relationship shall be

reported. We expect inspections will take due account of this situation in order to ensure appropriate reporting by pharmaceutical companies.

Simplify and make proportional to risk periodic safety update report submission by industry (PSURs)

PGEU welcomes the periodic safety update reports as we consider it will strengthen medicine safety and provide extensive and accurate information after a product is authorised.

Strengthen medicines safety transparency and communication

Centralised coordination regarding medicines safety by EMEA could make reporting and decision taking more effective, rapid and transparent.

PGEU would like to stress that health professionals need to be equipped with certain information before safety issues are reported in the mass media to the general public, in order to avoid unnecessary crises. Early involvement of health professionals in communication regarding safety issues could enable them to advise and clarify the situation to patients more effectively and in full synergy with competent authorities. Therefore it is important not only to focus on how to promote public access to the EMEA web-based information but similarly important to discuss and develop communication flows taking into consideration the additional resource health professionals can represent. Likewise, healthcare professionals would certainly benefit from having feedback on what they report.

An important aspect which seems to have been left out is the fact that at present, at least in the case of community pharmacists, there are existing pharmacy-based information systems with functionalities including safety alerts. These systems could be enhanced if prior to formal authorisation and in advance of launching the medicine in the market, the information submitted by the applicant in relation to the SPC and PIL would be made available for updating those systems.

One particular area which is of extreme importance and is not addressed so far in the legislative proposal is how risks and side effects are communicated to the general public and to individual patients. The role of the different agents involved in the pharmacovigilance system should be clarified with regards to this specific communication aspect.

Considering the fact that the legislator wants to emphasise transparency we do not understand the suggestion of having to ask for the agreement of the manufacturer for making publicly available an amended abstract of a post-authorisation study [(Article 101h(j)]. What happens if the marketing authorisation holder does not agree? The abstract is not published? Such a refusal should also be made public.

Clearer safety warnings in product information to improve the safe use of medicine

We recognise the importance of delivering simplified and highlighted key messages via patient information leaflet. This equips the patient with appropriate knowledge and draws attention to the most important messages in an adequate language.

PGEU believes that there should be a message encouraging the patient to discuss with their doctor or pharmacist adverse affects that occur during medication whether they are described or not in the patient information leaflet.

3. Other changes worth noting

- We agree with the simplification of the definition of "adverse reaction" [Article 1(11)] but we are not favourable to the deletion of the definition of "unexpected adverse reaction" [Article 1(13)].

- We agree with the amendment to the definition of "post-authorisation safety study" [Article 1(15)] and we welcome the introduction of the terms "Risk management system" [Article 1(33)] and "Pharmacovigilance master file" [Article 1(34)] and they bring additional clarification.

- The proposed change in Article 26, suggesting the deletion of the condition to refuse the marketing authorisation on the bases that "its therapeutic efficacy is insufficiently substantiated by the applicant", is, to say the least, a curious one. The amendment is of course consistent with the possibility of having medicinal products authorised earlier in their development. However, it is unacceptable that a medicine is authorised if the applicant cannot at least justify its ***therapeutic efficacy***.

  The basic principle for authorising a medicine is to ensure its quality, safety and efficacy. The overall proposed changes are already touching limit areas with regards to safety. To step in into the efficacy area as well may seriously endanger such basic principle.

Commission Proposal	**Suggested text by PGEU**
Article 26	**Article 26**
1. The marketing authorisation shall be refused if, after verification of the particulars and documents listed in Articles 8, 10, 10a, 10b and 10c, it is clear that: (a) the risk-benefit balance is not considered to be favourable; or ~~(b) its therapeutic efficacy is insufficiently substantiated by the applicant; or~~ (b) its qualitative and quantitative composition is not as declared.	**No change to the current text of the legislation** 1. The marketing authorisation shall be refused if, after verification of the particulars and documents listed in Articles 8, 10, 10a, 10b and 10c, it is clear that: (a) the risk-benefit balance is not considered to be favourable; or (b) its therapeutic efficacy is insufficiently substantiated by the applicant; or (c) its qualitative and quantitative composition is not as declared.

- We note that the European Commission suggests replacing title IX of Directive 2001/83/CE with a full set of articles, which, in essence, gives a much bigger role and responsibility to the pharmaceutical industry to the detriment of national competent authorities.

- The text contained in the current Article 102 is completely removed. We are opposed to this deletion as it clearly states the importance of having in place a pharmacovigilance system (covering all authorised medicines), at Member States' level and we would like to have it reinserted as a first point of Article 101b.

Commission Proposal	**Suggested text by PGEU**
Article 101b	**Article 101b**
1. Following consultation with the Agency, Member States and interested parties, and in accordance with the procedure referred to in Article 121 (2), the Commission may adopt guidelines on good pharmacovigilance practice including technical rules and procedures for: (…) 2. Marketing authorisation holders, the Agency and the competent authorities shall follow the guidelines	***1. In order to ensure the adoption of appropriate regulatory decision concerning the medicinal products authorized within the Community, having regard to information obtained about adverse reactions to medicinal products under normal conditions of use, the Member States shall have in place a pharmacovigilance system. This system shall be used to collect information useful in the surveillance of medicinal products,***

referred to in paragraph 1 in the fulfilment of their tasks related to pharmacovigilance . 3. The measures adopted shall take account of international harmonisation work carried out in the field of pharmacovigilance.	***with particular reference to adverse reactions in human beings, and to evaluate such information scientifically.*** ***Such information shall be collated with data on consumption of medicinal products.*** ***This system shall also take into account any available information on misuse and abuse of medical products which may have an impact on the evaluation of their benefits and risks.*** ***2.*** Following consultation with the Agency, Member States and interested parties, and in accordance with the procedure referred to in Article 121 (2), the Commission may adopt guidelines on good pharmacovigilance practice including technical rules and procedures for: (…) ***3.*** Marketing authorisation holders, the Agency and the competent authorities shall follow the guidelines referred to in paragraph 1 in the fulfilment of their tasks related to pharmacovigilance. ***4***. The measures adopted shall take account of international harmonisation work carried out in the field of pharmacovigilance.

- The proposed Article 101g(10) states that "the competent authority which granted the marketing authorisation may require a marketing authorisation holder to conduct a post-authorisation safety study if there are serious concerns about the risks affecting the risk-benefit balance of an authorised medicinal product." We do not understand how a marketing authorisation can be granted if there are ***serious concerns*** about the risks affecting the risk-benefit balance of the medicinal product.

- The database to which Article 123(4) relates is currently managed on an annual basis. It would be sensible if this database, which shall be run by EMEA in the future, contained updated data on a daily basis and would also be accessible to all agents involved in the pharmacovigilance process. Moreover, the database should not only cover medicines which are prohibited, but also those whose authorisation is temporarily suspended.

4. Final remarks

Taking account of the following:

- EMEA recognises that under reporting continues to be a problem;
- Under reporting and biased reporting of adverse events are as common in children as in adults, if not more so;
- Some countries only allow doctors to report;
- Large, observational databases will be essential to the safe use of medicines in children and other specific groups of the population.
- Data collection will remain difficult without more incentives for health care practitioners to use computers as an aid to clinical management and without the removal of certain laws that prevent different health care professionals from keeping long term records;

and in view of

- pharmacists' professional degree course, practice experience and continuing professional development leading to comprehensive pharmaceutical knowledge;
- the place of pharmacists in the pan-European patient / medical care interface;
- the ease of access and geographic distribution of pharmacy premises;
- the importance to the public of the dispensing and advisory roles of pharmacists;
- the level of computerization of community pharmacies;
- the pharmacist's role in early identification of adverse drug reactions;

the PGEU believes that community pharmacists, through the broad network of pharmacies throughout all Member States of the EU, are a useful and highly accessible resource that should be used to its full potential in the development of national pharmacovigilance systems.

END