Europejski Rzecznik
Praw Obywatelskich

Decyzji w sprawie 2370/2005/OV - Zarzut braku informacji dotyczących środka antydepresyjnego

Decyzja
Sprawa 2370/2005/OV - **Otwarta** 18/07/2005 - **Decyzja z** 05/12/2007

Mąż skarżącej popełnił samobójstwo w okresie, gdy zażywał środek antydepresyjny Seroxat/Paroxetine. Po śmierci męża skarżąca skontaktowała się z Europejską Agencją Leków w sprawie bezpieczeństwa tego leku oraz związanego z nim ryzyka samobójstwa. Skarżąca domagała się - między innymi - informacji o naukowej opinii Agencji na temat tego leku. Jednakże niektóre z wiadomości przesłanych przez nią drogą elektroniczną pozostały bez odpowiedzi. Skarżąca uznała również, że odpowiedzi nadesłane przez Agencję są niezadowalające. W skardze do Rzecznika skarżąca zarzucała: brak przejrzystości i informacji ze strony Agencji w odniesieniu do jej żądań; nadmierną zwłokę w udzieleniu odpowiedzi; niezapoznanie się z jej stanowiskiem w kwestii bezpieczeństwa leku i związanego z nim ryzyka samobójstwa; oraz brak działań Agencji w związku z jej zastrzeżeniami.

W swojej opinii Agencja argumentowała, że na niektóre zapytania skarżącej przesłane pocztą elektroniczną nie odpowiedziała, ponieważ powtarzały się i były bezcelowe. Agencja oświadczyła, że w odpowiedzi na pozostałe udzieliła skarżącej wszelkich niezbędnych informacji.

Po starannej analizie stosownej korespondencji Rzecznik doszedł do wniosku, że Agencja nie odpowiedziała na trzy pytania zadane przez skarżącą. Dlatego też zaproponował rozwiązanie polubowne i poprosił Agencję o (i) złożenie przeprosin z powodu uznania części wiadomości elektronicznych wysłanych przez skarżącą za powtarzające się i bezcelowe oraz (ii) udzielenie odpowiedzi na przedmiotowe pytania. Agencja przyjęła propozycję Rzecznika, przeprosiła skarżącą i odpowiedziała na te trzy pytania.

W swojej decyzji Rzecznik wyraził zadowolenie z powodu przyjęcia jego propozycji przez Agencję. Biorąc jednak pod uwagę, że skarżąca nadal była niezadowolona z pisma z przeprosinami oraz z otrzymanych odpowiedzi na swoje pytania, doszedł do wniosku, że osiągnięcie rozwiązania polubownego nie jest możliwe. Niemniej jednak Rzecznik uznał, że ponieważ działanie podjęte przez Agencję oddaliło stwierdzone przez niego wątpliwości, nie zachodzi już niewłaściwe administrowanie przez Agencję.

Co do zarzutu, że skarżąca nie została wysłuchana i że brak było działania ze strony Agencji, Rzecznik stwierdził, na podstawie analizy procedury obowiązującej w przypadku wydania

pozwolenia na dopuszczenie leku do obrotu, że nie wystąpiło niewłaściwe administrowanie przez Agencję. Dlatego też Rzecznik zamknął sprawę.

Strasbourg, 5 December 2007
Dear Mr O.,

On 27 June 2005, you made a complaint to the European Ombudsman concerning an alleged lack of transparency and information by the European Medicines Agency (the "Agency") with regard to the Agency's review of Paroxetine containing medicines. On 3 July 2005, you sent additional documents concerning your complaint.

On the same day you also made another complaint concerning the same matter against the European Commission with the same allegations. This complaint has been the subject of a separate inquiry under reference 2371/2005/OV and you will be informed of the outcome of this inquiry in a separate letter.

On 18 July 2005, I forwarded the complaint to the Executive Director of the Agency.

On 25 July 2005, I received a letter dated 13 July 2005 from Mr Brian Crowley MEP who wrote to lend support to your complaint. I replied to Mr Crowley on 30 August 2005, pointing out also that he would be kept informed of the outcome of your complaint. A copy of the present decision will therefore be sent to him for information.

On 27 August, 9 September 2005 and 17 October 2005, you sent three e-mails concerning your complaint. The first one included a copy of a recent study concerning Paroxetine, and the two latter ones copies of your correspondence with the Chief Executive Officer of the National Irish Medicines Board. In my reply of 3 November 2005, I informed you that I considered it preferable to wait for the Agency's opinion on your complaint before deciding whether further steps needed to be taken with regard to these e-mails.

The Agency sent its opinion on 26 October 2005. I forwarded it to you with an invitation to make observations, which you sent on 3 December 2005.

You sent further e-mails to my office on 10 December 2005 (two e-mails) and 11 March 2006 concerning both the present complaint and complaint 2371/2005/OV.

Afterwards, on a very regular basis, you continued to send voluminous e-mails to a list of 20 to 40 addresses, including my office. In these e-mails, you forwarded further reports, studies, articles as well as newspaper extracts concerning the issue of drug safety, and in particular Selective Serotonin Reuptake Inhibitors (SSRIs) and Paroxetine. These e-mails were registered under the reference of both the present complaint and complaint 2371/2005/OV.

You sent these e-mails (more than hundred in total) on the following dates: on 22 and 26 April 2006, on 6 (three e-mails) 7, 13 and 16 (two e-mails) May 2006, on 4, 8, 21, 25 and 27 (two e-mails) June 2006, on 3, 4, 6, 8 (two e-mails), 11, 19, 21, 22, 23, 25 and 29 July 2006, on 27

(three e-mails), 28, 29 (two e-mails) and 30 August 2006, on 7, 8, 12, 14, 20, 22, 23, 24, 28 and 30 September 2006, on 8, 13, 18 and 28 October 2006, on 6 (three e-mails), 8, 24, 26, 27, 28 and 30 November 2006, on 5 (two e-mails), 6 (two e-mails), 9 (two e-mails), 15, 16 and 18 (three e-mails) December 2006, on 7 (three e-mails), 8, 14, 19, 20, 21, 23 (two e-mails), 24, 26, 28, 29 (four e-mails) and 30 (three e-mails) January 2007, on 1, 2, 5, 7, 15, 17, 24 and 27 February 2007, on 13, 18, 19, 22, 23 (two e-mails) and 30 March 2007, and on 1, 2, 3 (two e-mails), 4 (two e-mails), 6 and 30 April 2007, and on 14 June 2007.

On 4 July 2007, my Office contacted you in order to explore the possibility of a friendly solution with regard to your complaint.

On 26 July 2007, I addressed a proposal for a friendly solution to the Agency. You were informed accordingly in a letter of the same day.

The Agency sent its reply regarding the proposal for a friendly solution on 1 October 2007. On that date, the Agency also sent a letter of apology directly to you. On 2 October 2007, you sent me your observations on the Agency's letter of apology. On 3 October 2007, you had a telephone conversation with my Office. On 12 October 2007, I forwarded the Agency's reply of 1 October 2007 to you with an invitation to make observations by 15 November 2007. In a telephone conversation with my Office on 13 November 2007, you indicated that you would not make further observations on the Agency's reply and that your observations on the Agency's letter of apology constituted also your observations on the Agency's reply to the Ombudsman.

I am writing now to let you know the results of the inquiries that have been made.

I apologise for the length of time it has taken to deal with your complaint.

THE COMPLAINT

The complainant is an emergency nurse in Cork University Hospital. According to the complainant, the relevant facts of the case are, in summary, as follows:

On 26 December 2003, and at the age of 39 years, the complainant's husband and father of her three children, committed suicide while taking Seroxat (1) /Paroxetine. According to the complainant, Seroxat caused her husband to commit suicide. After her husband's death, the complainant contacted the European Medicines Agency (hereafter "the Agency") with regard to the use, the dangers and warnings of Selective Serotonin Reuptake Inhibitors ("SSRIs") and Paroxetine in particular. In her e-mail of 12 January 2004, the complainant requested information regarding the Agency's scientific opinion on Paroxetine and any other information regarding the drug's safety and suicide risk. By e-mail of 19 January 2004, the Agency informed the complainant that her e-mail had been forwarded to its Document Management and Publishing Sector, but the latter never replied.

On 9 May 2004, the complainant contacted the European Commission by e-mail and requested

a copy of the full review, findings and recommendations of the Agency on Paroxetine, as well as explanations regarding the procedure for the ratification of the Agency's recommendations by the Commission. The complainant also pointed out that she wanted to be heard before the Commission adopted its final decision. By e-mail of 25 May 2004, the Commission replied that the complainant should address her questions to the Agency and gave her the contact details of an official in the Agency.

On 27 May 2004, and after contacting the office of the former President of the European Parliament, Mr Pat Cox, the complainant contacted the said Agency's official. On 11 June 2004, another official of the Agency, without providing any apology for the delay, replied to the complainant's e-mail addressing some issues raised by the complainant. However, that official refused to provide more detailed information on the scientific conclusions and grounds for the opinion and recommendations of the Agency's CHMP (Committee for Medicinal Products for Human Use) until the Commission had adopted relevant recommendations. The complainant was still waiting for detailed information from the Agency on the scientific conclusions and grounds for the CHMP opinion, even though the Commission had taken its final decision on this issue. Furthermore, the official failed to give the complainant the opportunity to share her personal experience and anecdotal evidence, as the Agency had already heard a group of Paroxetine users.

The complainant replied by e-mail of 11 June 2004 and pointed out that the Agency had not reviewed unpublished data regarding Paroxetine, data of clinical trials and a wide range of anecdotal evidence, including her own experience. She asked various questions and stated that, in the interest of public safety, the Agency and the CHMP should reconsider the matter and try to obtain all data from the pharmaceutical companies. The complainant did not receive an answer and e-mailed again on 6 July 2004 and 23 August 2004. The Agency's official replied to her on 5 October 2004, that is, 87 days after the complainant's last unanswered e-mail. In his reply, the official did not apologise for the delay and refused to release the more detailed information that the complainant had requested. The official also informed her that her questions concerning suicide warnings would be brought to the attention of the CHMP, which would consider the issue in its next plenary meeting of 19-21 October 2004. On 18 November 2004, the Chairman of the CHMP replied to the complainant. The complainant considers that his response was inadequate and impersonal and did not give specific consideration to her concerns and questions. The complainant also considered the letter arrogant, patronising, unaccountable and dismissive.

On 26 November and 8 December 2004, the complainant e-mailed new information to the Agency concerning warnings and guidelines that antidepressants should not be used by mildly depressed patients, but the complainant's e-mails were not answered.

The complainant is extremely concerned at what she perceives to be the failings of the Agency to protect EU citizens from preventable drug-induced harm and points out that these concerns were also expressed by the Executive Director of the Agency himself. According to the complainant, the regulation of SSRIs antidepressants remains chaotic and misconceived, thereby causing further harm. In her view, the Agency was set up to protect the public, but it has

ended up protecting the pharmaceutical companies.

On 27 June 2005, the complainant lodged the present complaint with the Ombudsman concerning alleged maladministration by the Agency. In her complaint, she pointed out that the Agency had not respected the European Code of Good Administrative Behaviour. On the basis of the complaint form and the additional explanations in the accompanying letter, the complainant's allegations can be summarised as follows:
- There has been a lack of transparency and information by the Agency and its CHMP with regard to the complainant's request for their review on Paroxetine and any other information regarding the safety and suicide risk of SSRIs and Paroxetine in particular.
- There has been undue delay in the replies to the complainant's e-mail correspondence.
- The complainant was not heard by the Agency with regard to the matter of the safety and suicide risks of Paroxetine and her opinion was not taken into account. Also, there was a lack of action by the Agency regarding her concerns.

THE INQUIRY

The European Medicines Agency's opinion

In its opinion, the Agency made, in summary, the following comments:

Starting with an e-mail dated 12 January 2004, the complainant wrote several letters and e-mails to the Agency. Her first request was aimed at obtaining information " *on the review of Paroxetine/Seroxat made by the [Agency] (...) or any relevant works concerning safety and suicide risk of the drug* ". Ms L. from the Agency's Document Management Sector replied to this message on 19 January 2004, that is, within five working days of 12 January 2004 and thus within the two-week deadline foreseen in Article 14 (acknowledgement of receipt and indication of the competent agent or other servant) (2) of the Agency's Code of Good Administrative Behaviour (3) . The complainant was advised to contact the specific section of the Agency's website which contains all the information that can be disclosed to the general public.

On 27 May 2004, the complainant contacted the Agency for a second time, by sending an e-mail to Mr T., the Head of Sector for the Pharmacovigilance and Post-Authorisation Safety & Efficacy of Medicines in the Post-Authorisation Human Unit. Mr T.'s name had been suggested to the complainant by Mr A. of the Commission to whom the complainant had sent a previous e-mail. In her second message, the complainant requested access " *to the full review* "; asked for information concerning further procedural steps related to the Agency or the CHMP's review on Paroxetine; and expressed her interest in being heard " *before the Commission passes its decision* ".

The Agency recalled that at this stage, on 22 April 2004, the CHMP (under its former name "CPMP" (4)) completed its EU-wide review for medicines containing Paroxetine. The review was initiated by the United Kingdom in June 2003 under Article 31 (referral procedure) of the Community Code on human medicines (Directive 2001/83/EC (5)).

The outcome of this review, as reported below, was immediately made public by way of a press

release, which appeared on the Agency's website on the same day (Doc. Ref. EMEA/D/11206/04/Final) and by a Question and Answers Document on Paroxetine published the following day. As extrapolated from the press release, the Committee concluded that the risk-benefit assessment for medicines containing Paroxetine remained positive, but made the following recommendation:

" *The Committee recommends that Paroxetine should not be used in children and adolescents as clinical trials have found Paroxetine to be associated with increased risk of suicidal behaviour and hostility. In addition, trials in children and adolescents did not adequately demonstrate efficacy. The Committee noted that Paroxetine is not authorised in any EU Member State for use in children.*

There is a possibility of an increased risk of suicide-related behaviour in young adults. As a consequence young adults should be monitored carefully throughout treatment.

The Committee also recommends strengthened warnings concerning withdrawal symptoms. Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt and the Committee underlines that patients must not stop their treatment abruptly, except on medical advice ".

With regard to the specific requests submitted by the complainant in her e-mail of 27 May 2004, the Agency noted that:
- The content of the full report concerning the assessment of the relevant medicinal product (Seroxat) could not be disclosed at that stage, that is, at the time when the Committee issued its opinion. The Background Information on the procedure together with the annexes of the CHMP opinion describing the scientific conclusions and the recommended changes to the product information could be published only after the Commission had adopted its final decision. The Commission adopted its final decision on 29 March 2005. According to the relevant legal provision, new questions of a scientific or technical nature may be raised by Member States during the decision-making phase which may oblige the CHMP to reconsider its scientific opinion before the Commission issues its decision. This latter clarification was provided to the complainant as part of the Agency's e-mail of 11 June 2004.
- The relevant legal provisions of the pharmaceutical legislation do not grant individuals the right to be heard in the framework of the assessment procedure. The representatives of the CHMP and the Agency nevertheless heard the scientific concerns expressed by a group of user patients as opposed to a single individual. Furthermore, the CHMP Chairman decided to send the complainant a follow-up letter which was dated 18 November 2004.

The e-mail sent to Mr T. on 27 May 2004 was answered by his immediate superior, Mr W., on 11 June 2004, that is, within 11 working days and thus within the two-week deadline foreseen in Article 14 of the Agency's Code of Good Administrative Behaviour. The reply provided the complainant with detailed information concerning the EU-wide review on Paroxetine and clear indications on the follow-up procedure.

The Agency also pointed out that it is clearly stated in Article 14 of its Code that " *[e]very letter*

or complaint to the Agency shall receive an acknowledgement of receipt within a period of two weeks, except if a substantive reply can be sent within that period. (...) ". In the present case, the complainant did not receive any acknowledgement of receipt, because she got a substantive reply within the two-week period.

The complainant addressed further e-mails to Mr W. on 11 June, 6 July and 23 August 2004. In these messages, the complainant complained about the alleged lack of consideration, in the assessment by the CHMP, of " *unpublished data regarding Paroxetine, the raw data of clinical trials, unavailable clinical trials and a wide range of anecdotal evidence (including my own)* ".

In the same context, the complainant also asked to know whether the CHMP had (i) requested " *all data from all clinical trials carried out by GlaxoSmithKline (GSK) on Paroxetine* "; (ii) sought an explanation on " *the difference on warnings of the same drug in the USA/Canada/EU* "; (iii) proposed to refer the issue back to the CHMP for further consideration; (iv) asked whether the Commission had already prepared a draft decision and (v) asked whether any Member State had raised " *important new questions of a scientific or technical nature, which have not been addressed in the opinion of the EMEA/CHMP* ".

The first two messages were not acknowledged or replied to as they were considered repetitive and pointless. The decision not to acknowledge or reply was taken in accordance with Article 14 of the Agency's Code of Good Administrative Behaviour which provides that " *(...) No acknowledgement of receipt and no reply need be sent in cases where letters or complaints are abusive because of their excessive number or because of their repetitive or pointless character.* "

A substantive reply to the complainant's e-mail of 23 August 2004 was nevertheless sent to the complainant on 5 October 2004, as soon as the agenda of the next CHMP plenary meeting was fixed. In this reply, the complainant was informed that her specific scientific questions concerning the suicide warning had been tabled for discussion at the next CHMP plenary meeting.

The outcome of the CHMP discussion of November 2004 was promptly reported to the complainant in a letter of 18 November 2004 from the Chairman of the CHMP. This letter reproduced the content of the warnings that the CHMP recommended for inclusion in the product information concerning medicines containing Paroxetine and relating to suicidal thoughts and behaviour.

This was followed by an exhaustive press release (Ref. Doc. EMEA/192570/2004) and by a revised version of the Questions and Answers Document on Paroxetine (Doc. Ref. EMEA/192942/2004). Both documents were published on the Agency's website on 9 December 2004. The updating of the Questions and Answers Document on Paroxetine was required to reflect the assessment of additional scientific data submitted during the decision-making phase. It should nevertheless be stressed that the CHMP, after the assessment of this additional scientific data, re-confirmed its scientific conclusions on the risk-benefit of medicines containing Paroxetine, which were initially described in its opinion of 22 April 2004.

The Agency concluded that, in light of the documentary evidence provided by the complainant and of additional documents attached to the Agency's opinion, it had acted in accordance with the provisions set out by both the relevant applicable legislation and its own Code of Good Administrative Behaviour. In particular, it had respected the rules concerning the disclosure of information relating to safety issues as regards marketed medicinal products, the procedure and deadlines for replies to queries received from the general public and the need to ensure that the CHMP performs its duty of assessment in full autonomy and independence.

The complainant's observations

The complainant's observations can be summarised as follows:

The complainant accepted the Agency's opinion with regard to Ms L.'s e-mail of 19 January 2004 and stated that it had provided the necessary clarifications. She indicated that it was initially not very clear to her that Ms L. worked within the Document Management and Publishing Sector of the Agency and that, therefore, she assumed that Ms L. had forwarded her e-mail to the relevant department which was to send her a full reply.

With regard to Mr T.'s e-mail of 27 May 2004, the complainant wondered why Mr T. replied to the secretary of Mr Pat Cox, whom the complainant had contacted in relation to this matter, within a couple of hours whilst Mr T. took 15 days to reply to her.

The complainant stated that she was still waiting for detailed information on the scientific conclusions and grounds for the CHMP opinion.

As regards the Agency's position that there was no legal ground to grant her the right to be heard in the framework of the assessment procedure, the complainant observed that the Agency/CHMP nevertheless heard scientific concerns expressed by a group of Seroxat user patients. The complainant attached to her observations two reports of the meeting of 19 April 2004 held at the Agency's premises (6) . During the meeting, the Agency made it clear that it was not standard practice to listen to patients' scientific concerns. According to the complainant, this was merely an attempt to seek publicity. The complainant observed that the review was completed and a press release was issued on 22 April 2004, merely three days after the meeting with the Seroxat User Group about their scientific concerns. According to the complainant, this indicates that it was never the intention of the CHMP to pay any attention to what the Seroxat User Group had to say. The complainant emphasised that there was something fundamentally wrong if the Agency did not have a responsibility to listen to the individuals who are the clinical experts in the field. However, the Agency appeared to listen to pharmaceutical companies.

According to the complainant, the Agency is leaning more towards its licensing role than towards its duty of pharmacovigilance to protect public health. This tendency is different, for instance, to that of the Food and Drug Administration ("FDA") in the United States. The FDA, when assessing the safety of SSRIs, listens to anecdotal cases presented by various individuals or their families and the evidence obtained may lead the FDA to issue warnings.

The fact that the Agency listens more to pharmaceutical companies has the consequence that

the regulatory bodies issue licenses for drugs solely on the basis of pharmaceutical "summaries" of clinical trials whose accuracy cannot be verified. The data which are used originate from the pharmaceutical industry and from the published literature which is often sponsored by the industry itself.

The complainant also referred to a United Kingdom Parliamentary report on various shortcomings of the Medicine and Healthcare Products Regulatory Agency ("MHRA") in the United Kingdom. This report revealed major failings in the regulatory system: the organisation, procedures and techniques of the MHRA are focussed on putting drugs on the market as quickly as possible; the process by which drugs are licensed is far from transparent; there is not enough involvement from patients; and the MHRA does not listen or communicate well. The complainant observed that the same findings could be made with regard to the Agency.

According to the complainant, the regulatory body should randomly audit unprocessed data, and the drug safety monitoring system should operate independently from the licensing authority. When problems arise after a drug has been put on the market, the regulators should examine their own failings and a public inquiry should be conducted because such cases often involve drug-induced problems for users.

As regards Mr W.'s reply of 11 June 2004 to her e-mail of 27 May 2004, the complainant observed that Mr W. addressed some issues mentioned in her complaint, but failed to answer the most important questions such as: (i) did the CHMP request *all* data from *all* clinical trails carried out by GlaxoSmithKline ("GSK") on Paroxetine? (ii) How do you explain the differences of warnings for the same drug in the United States, Canada and the EU? (iii) Why is the Agency, in the interest of public safety, not battling to obtain *all data* from the pharmaceutical companies?

As regards the fact that the Agency did not answer her e-mails of 11 June 2004 and 6 July 2004 because they were regarded as abusive, the complainant considered this to be insulting, given that the relevant e-mails were necessarily repetitive because her questions had not been answered. According to the complainant, Article 14 of the Agency's Code of Good Administrative Behaviour is merely a means to avoid having to answer questions.

According to the Agency's opinion, Mr W.'s reply of 5 October 2004 to the complainant's e-mail of 23 August 2004 was substantive. In this reply, the Agency informed the complainant that (i) her " *specific scientific questions concerning suicide warnings* " would be brought to the attention of the CHMP, which would consider the issues in its plenary meeting of October 2004, and that (ii) she would receive a reply following this meeting. The complainant however observed that she was never informed of the discussions and the outcome of the meeting, and that therefore the Agency's position that the outcome of the November CHMP discussion was promptly reported to her was inaccurate and false. The complainant does not know whether discussions took place regarding her specific questions concerning suicide warnings. The Chairman's reply of 18 November 2004 does not indicate any discussion of her specific questions concerning suicide warnings. The complainant stated that, in her opinion, this letter would qualify as abusive under Article 14 of the Agency's Code of Good Administrative Behaviour.

The complainant further indicated that she sent a reply to the Agency in order to convey her dissatisfaction with how her case was being handled by its services and more importantly with the fact that no consideration was given to the health safety issue for the people in the European Union. According to the complainant, the foreseeable problems with the warning proposed by the Agency were the following: (i) there is no mention of the possible link between the drug and suicide or aggression; and (ii) the warning does not include all ages, but only up to the age of 30, and is sometimes at variance with warnings released by GSK itself in the United States and Canada.

The complainant attached to her observations, two reports from the meeting with the Seroxat User Group on 19 April 2004 and a memo of GSK of October 1998.

Further correspondence from the complainant

After having sent her observations, the complainant sent more than a hundred e-mails to the Ombudsman's Office and to other addresses, and, in addition, forwarded further reports, studies, articles as well as newspaper extracts concerning the issue of drug safety, and in particular SSRIs and Paroxetine.

THE OMBUDSMAN'S EFFORTS TO ACHIEVE A FRIENDLY SOLUTION

The Ombudsman's proposal for a friendly solution

After careful consideration of the Agency's opinion and the complainant's observations, the Ombudsman was not satisfied that the Agency had responded adequately to the complainant's allegations.

This view was based on the following considerations:

1 Preliminary remark and scope of the Ombudsman's inquiry

1.1 The European Ombudsman notes that the present complaint (7) , in which the complainant made three allegations against the European Medicines Agency (the "Agency") about the way it had reacted to her various requests and e-mails, as well as to her concerns, originates in the suicide of her husband and the father of her three children on 26 December 2003, at a young age.

The Ombudsman realises that the complainant has, over the past four years, gone through an extremely difficult time in her life and that, unfortunately, whatever the outcome of the present inquiry into her complaint, the complainant's personal situation as a result of that tragic event cannot be undone. The Ombudsman wishes to convey to the complainant his deepest sympathy for her loss and his kind wishes for her future and that of her family.

1.2 The Ombudsman notes that, in her observations, the complainant referred to various shortcomings that she considers to exist as regards the United Kingdom authorities in general and, in particular, the Medicine and Healthcare Products Regulatory Agency (the "MHRA"). The Ombudsman would like to underline that he can only investigate alleged instances of maladministration by Community institutions and bodies, and that he has no power to

investigate alleged maladministration by national authorities of the Member States. The present inquiry will therefore deal only with the alleged maladministration by the Agency.

1.3 The Ombudsman notes that, after having sent her observations on the Agency's opinion, the complainant sent a considerable number of further e-mails. The Ombudsman has carefully analysed this correspondence. However, it appears that these e-mails do not contain information the investigation of which would be necessary in order to deal with the complainant's allegations. The complainant's correspondence has however been added to the file, for information.

2 The alleged lack of transparency and lack of information

2.1 The complainant alleged that there has been a lack of transparency and information by the Agency and its Committee for Medicinal Products for Human Use ("CHMP") with regard to her request for the review undertaken by the Agency and the CHMP on Paroxetine and any other information regarding the safety and suicide risk of SSRIs and of Paroxetine in particular.

2.2 In its opinion, the Agency gave an overview of the correspondence it had with the complainant and of the content of its correspondence. It stated that it had advised the complainant to visit the specific section of its website which contained all the information that could be disclosed to the general public. The Agency stated that the outcome of the CHMP's review on medicines containing Paroxetine was immediately published by way of a press release which appeared on the Agency's website on 22 April 2004, and by a Questions and Answers Document published the following day.

The content of the full report concerning the assessment of the relevant medicinal product (Seroxat) could not be disclosed at that stage, that is, at the time when the Committee issued its opinion. The Background Information on the procedure together with the annexes of the CHMP's opinion describing the scientific conclusions and the recommended changes to the product information could only be published after the Commission had adopted its final decision. This final decision was adopted on 29 March 2005. According to the relevant legal provisions, new questions of a scientific or technical nature may be raised by the Member States during the decision-making phase which might result in the need for the CHMP to reconsider its scientific opinion before the Commission issues its final decision. The Agency provided this latter clarification to the complainant in its e-mail of 11 June 2004.

The Agency further stated that the outcome of the CHMP discussion of November 2004 was promptly reported to the complainant in a letter of 18 November 2004 from the CHMP's Chairman. This letter reproduced the content of the warnings that the CHMP recommended for inclusion in the product information for medicines containing Paroxetine and relating to suicidal thoughts and behaviour. This was followed by an exhaustive press release (Ref. Doc. EMEA/192570/2004) and by a revised version of a Question and Answers Document on Paroxetine (Doc. Ref. EMEA/192942/2004). Both documents were published on the Agency's website on 9 December 2004.

The Agency concluded that, in light of the documentary evidence provided by the complainant and of additional documents attached to its opinion, it had acted correctly. In particular, it had

acted in accordance with the provisions set out by both the relevant applicable legislation and its own Code of Good Administrative Behaviour with regard to the disclosure of information relating to safety issues as regards marketed medicinal products.

2.3 In her observations, the complainant stated that she was still waiting for detailed information on the scientific conclusions of CHMP's opinion and on the grounds underpinning it.

The complainant stated that Mr W.'s reply of 11 June 2004 to her e-mail of 27 May 2004 addressed some issues mentioned in her complaint, but failed to answer the most important questions, such as: (i) did the CHMP request *all* data from *all* clinical trails carried out by GlaxoSmithKline (GSK) on Paroxetine? (ii) How do you explain the differences of warnings for the same drug in the United States, Canada and the EU? (iii) Why is the Agency, in the interest of public safety, not battling to obtain *all data* from the pharmaceutical companies?

The complainant further observed that she was never informed of the discussions and of the outcome of the meeting of November 2004, and that therefore the Agency's position that the outcome of the November CHMP discussion was promptly reported to her was inaccurate and false. The complainant stated that she did not know whether discussions took place regarding her specific questions concerning suicide warnings. The Chairman's reply of 18 November 2004 did not contain any discussion of her specific questions concerning suicide warnings. The complainant stated that, in her opinion, this letter would qualify as abusive under Article 14 of the Agency's Code of Good Administrative Behaviour.

2.4 The Ombudsman notes that, in order to deal with the complainant's allegation of lack of transparency and information by the Agency, a distinction should be made between, on the one hand, the complainant's requests for information and, on the other hand, her request for access to documents.

2.5 As regards, first, the complainant's requests for information, the Ombudsman notes that the complainant made her initial request in her e-mail of 12 January 2004 in which she asked " *[c]an you please send me information on the review of Paroxetine/Seroxat made by the EMEA? or any relevant works regarding safety and suicide risk of the drug* ". The Ombudsman notes that the Agency's Document Management and Publishing Sector, to which the complainant's e-mail had been forwarded, replied to the complainant on 19 January 2004. The Sector informed her that all public documents, including European Public Assessment Reports ("EPARs"), guidelines, concept papers and points to consider, are published on the Agency's website. The Agency provided the complainant with the link on its website to the EPARs on products given Marketing Authorisation via the Centralised Procedure.

2.6 The Ombudsman notes that, on 22 April 2004, the CHMP adopted its opinion concerning the review of medicines containing Paroxetine. On the same day, the Agency published a press release on its website (Doc. Ref: EMEA/D/11206/04/Final). The following day, the Agency also published a Questions and Answers Document. The Ombudsman notes that this last document was published in the context of the Agency's new transparency policy measures which were adopted in October 2003 (8) .

2.7 On 27 May 2004, the complainant sent a second e-mail to the Agency. In this e-mail, the complainant referred to the suicide of her husband. She also referred to the Agency's press release of 22 April 2004 on its review of Paroxtine containing medicines, which she considered rather vague. She asked what the next step in the procedure was, when the Commission would take its decision, and whether the CHMP had listened or would listen to individual cases (the complainant proposed to be heard herself) and take them into account in the final decision.

2.8 The Ombudsman notes that, on 11 June 2004, the Agency sent a two-page reply to the complainant's e-mail of 27 May 2004. In its reply, the Agency described how the review of medicines containing Paroxetine had been initiated, namely, via the referral procedure launched by the MHRA. The Agency also described the review procedure and stated that it had organised a meeting with the Seroxat User Group. Furthermore, the Agency referred to the opinion which the CHMP had adopted on 22 April and also reproduced the content of the recommendations made in that opinion. The Agency referred to the press release and the "Questions and Answers" Document which it had published on its website. The Agency went on to provide the complainant with further information on the decision-making procedure, more particularly on the steps to be taken between the adoption of the CHMP opinion and of the Commission decision. The Agency finally acknowledged the complainant's interest in sharing her personal experience, but stated that, given the current status of the formal procedure, it could reassure the complainant that, during its review, the CHMP had considered the available data on suicide, suicide attempts, suicidal ideation from clinical trials, as well as data derived from spontaneous reports and the published literature. It had also heard a group of Paroxetine users.

2.9 After having received the Agency's reply of 11 June 2004, the complainant replied the same day, expressing her disappointment with the Agency's review of medicines containing Paroxetine. The complainant referred to the fact that GSK had been forced to implement more explicit warnings concerning Seroxat in the United States and in Canada and asked how this could be explained. She also asked several other questions such as

" *did CHMP request all data from ALL clinical trials held by GSK before drawing their opinion for the adult population? (...) Has the Commission prepared a draft of the decision to be taken yet? (...) Has any Member State raised important new questions of a scientific or technical nature which have not been addressed in the opinion of the EMEA/CHMP?* "

On 6 July 2004, the complainant sent a further e-mail to the Agency. The Ombudsman notes that neither the e-mail of 11 June nor the one of 6 July 2004 was answered by the Agency. This issue is dealt with below in the section of the decision dealing with alleged undue delay.

2.10 On 23 August 2004, the complainant sent another e-mail in which she expressed her (critical) opinion about the Agency's review of medicines containing Paroxetine and stated that, " *if not corrected before passing it into law, [it] could endanger the health and safety of the European citizens over 30 that are prescribed this medicine without the appropriate warning* ". She also stated that she " *would appreciate a reply and an update about the proposed warning status if possible* ".

2.11 The Ombudsman notes that, in its reply of 5 October 2004, the Agency provided further information to the complainant. More particularly, the Agency stated that the decision on medicines containing Paroxetine had not yet been taken by the Commission and that the procedure was at the stage at which each Member State was allowed to forward written observations on the draft decision to the Commission. The Agency also stated that the complainant's specific questions concerning suicide warnings had been brought to the attention of the CHMP which would consider the issues at its plenary meeting of 19-21 October 2004. Furthermore, the Agency stated that " *thereafter a reply will be sent to you within a short period following the conclusion of that meeting* ". The Ombudsman notes that the plenary meeting was finally held on 15-18 November 2004 and that, on 18 November 2004, the Agency, in the person of the Chairman of the CHMP, indeed sent a further letter to the complainant, also in reply to her e-mail of 23 August 2004. In this letter, the Agency provided the complainant with further information and clarifications concerning the issues discussed by the CHMP at its meeting, and more particularly with information on the warnings concerning suicidal thoughts and behaviour which the CHMP agreed should be included in the product information for medicines containing Paroxetine (9) . The Agency further informed the complainant that

" *the above conclusions/recommendations of the CHMP have not yet been converted into a Commission Decision and therefore at this stage it cannot be granted that these will be the final recommendations. Once the Commission Decision has been issued, the CHMP final conclusions will be made publicly available* ".

2.12 The Ombudsman notes that, on 9 December 2004, the Agency published another press release on its website (Doc. Ref. EMEA/192570/2004) concerning the CHMP meeting of 8 December 2004 on Paroxetine (and other SSRIs), as well as a revised version of the Questions and Answers Document. It appears from this press release that, at the request of the Commission, the CHMP re-examined its opinion of 22 April 2004 on Paroxetine in light of additional information arising from newly available observational studies. Following the assessment of this additional information, the CHMP confirmed its initial conclusion that the risk-benefit balance for medicines containing Paroxetine remained positive in the treatment of adults. The CHMP also reaffirmed its previous conclusions that changes to the product information should be introduced, expecially with regard to warnings of suicide-related behaviour in children and adolescents. The CHMP included a document containing details of these findings.

2.13 On the basis of the above elements, the Ombudsman comes to the following conclusions. It appears that, in their four replies of 19 January, 11 June, 5 October and 18 November 2004, as well as in the framework of the present inquiry, the Agency and the CHMP provided the complainant with relevant information (or links to it). Further information was contained in the Agency's press releases and in the Questions and Answers Documents put on its website on 22 April, 23 April and 9 December 2004. The Agency also explained to the complainant in detail the procedures concerning the adoption of the decision on medicines containing Paroxetine, and replied to most of her questions. With regard to the general information concerning the review of Paroxetine, the Ombudsman notes that there has been no lack of transparency or lack

of information by the Agency.

2.14 With regard, however, to the complainant's specific questions set out in the complainant's e-mails of *11 June 2004* and of *6 July 2004* , the Ombudsman notes the following: First, the e-mail of *11 June 2004* , which contained several questions, remained unacknowledged and unanswered. The Ombudsman notes that, in its opinion, the Agency argued that, in accordance with Article 14 of its Code, no reply was needed, as it considered these e-mails to be repetitive and pointless. In this regard, the Ombudsman notes that in her e-mail of *11 June 2004* , the complainant reacted to the Agency's detailed reply of 11 June 2004 and asked several questions such as

" *did CHMP request all data from ALL clinical trials held by GSK before drawing their opinion for the adult population? (...) Has the Commission prepared a draft of the decision to be taken yet? (...) Has any Member State raised important new questions of a scientific or technical nature which have not been addressed in the opinion of the EMEA/CHMP?* "

Given that a Commission Decision had not yet been taken at that time, it does not appear that the complainant's questions were pointless. It also appears that the Agency had not yet replied to these questions on an earlier occasion. Second, the Ombudsman notes that, in her e-mail of *6 July 2004* , the complainant explicitly stated that she was still waiting for a reply and that she would like a response. Third, the Ombudsman takes the view that the exception concerning repetitive or pointless correspondence can be used only if the person concerned has been informed beforehand by the institution concerned of its intention to discontinue correspondence on that ground. Finally, the Ombudsman considers that, in these conditions, the Agency's submission that the complainant's e-mails were repetitive and pointless could indeed be perceived by the complainant as being insulting. On the basis of the above considerations, the Ombudsman's provisional conclusion is that the Agency's failure to reply to the complainant's e-mails of 11 June and 6 July 2004 constitutes an instance of maladministration. The Ombudsman therefore makes the proposal for a friendly solution below.

2.15 As regards the complainant's observation that the CHMP's Chairman's reply of 18 November 2004 did not indicate any discussion on her specific questions concerning suicide warnings, the Ombudsman considers that this aspect of the allegation appears to concern the complainant's right to be heard, which is dealt with below in point 4. As regards the complainant's comment that she found the Chairman's reply to be arrogant, patronising, unaccountable and dismissive, the Ombudsman has carefully analysed the content and wording of the letter, but has found nothing to justify such criticism.

2.16 As regards the complainant's request to be provided " *with a copy of the full review, findings and recommendations* " of the Agency on Paroxetine, the Ombudsman notes that the complainant's request was in fact part of her e-mail of 27 May 2004 which was a more general request for information. However, the Ombudsman considers that, although she did not formulate her request explicitly as a request for access to documents and although the Agency did not refer to its rules on access to documents, her request should be considered from the point of view of the rules applicable to requests for access to documents. In this respect, Article

23 of the Agency's Code provides that requests for access to documents held by the Agency shall be dealt with in accordance with its Decision on access to documents (10) .

2.17 The Ombudsman takes note of the Agency's reply of 11 June 2004 to the complainant's request to be provided with a copy of its full review, findings and recommendations on Paroxetine. In that reply, the Agency (i) referred to its press release of 22 April 2004 and to the Questions and Answers Document; and (ii) pointed out to the complainant that, as the CHMP's opinion had to be forwarded to the Commission which takes the final decision, it could not provide the complainant with the documents requested. The Agency added that

" *[m]ore detailed information on the scientific conclusions and grounds for the CHMP recommendations, including the full text of the product information for Paroxetine containing medicines as agreed by the CHMP, will be made public once the European Commission has issued its Decision on the basis of the CHMP Opinion* ".

The Agency repeated this statement in its replies to the complainant of 5 October and 18 November 2004.

2.18 The Ombudsman notes that, according to Article 3.3 of the Agency's Decision on access to documents,

" *[a]ccess to a document, produced or received and in possession of the Agency, which relates to a matter where the decision has not been taken, shall be refused if disclosure of the document would seriously undermine the decision-making process, unless there is an overriding public interest in disclosure* ".

The Ombudsman notes that, in its reply of 11 June 2004, the Agency did not refer to its Decision on access to documents. Nor did the Agency consider whether there was an overriding public interest in the disclosure of the documents requested by the complainant.

2.19 The Ombudsman notes however that the Commission's Decision on Paroxetine was finally adopted on 29 March 2005 and published in the Official Journal C 118 of 19 May 2005 (11) . The Ombudsman notes that the Commission's Decision contained as Annexes the full text of the revised CHMP's opinion of 8 December 2004, as well as the Summary of the Product Characteristics. The Ombudsman also notes that, in the framework of the inquiry in complaint 2371/2005/OV against the Commission, the complainant obtained a copy of the Commission's Decision and its annexes, which were attached to the Commission's opinion. Considering that the complainant has finally obtained access to the documents requested in her e-mail of 27 May 2004 to the Agency, there appear to be no grounds further to pursue the inquiry into this aspect of the case.

3 The alleged undue delay

3.1 The complainant alleged that there had been undue delay in the Agency's replies to her e-mail correspondence.

3.2 In its opinion, the Agency stated that the complainant wrote several letters and e-mails to

the Agency, starting with an e-mail of 12 January 2004. Ms L. from the Agency's Document Management Sector replied to this message, on 19 January 2004, that is, within five working days and thus within the two-week deadline foreseen in Article 14 of the Agency's Code. The complainant contacted the Agency for a second time on 27 May 2004, by sending an e-mail to Mr T., Head of Sector for the Pharmacovigilance and Post-Authorisation Safety & Efficacy of Medicines in the Post-Authorisation Human Unit. This e-mail was answered by Mr T.'s immediate superior, Mr W., on 11 June 2004, that is, within 11 working days and thus within the two-week deadline foreseen in Article 14 of the Agency's Code.

The Agency stated that the complainant then addressed further e-mails to Mr W. on 11 June, 6 July and 23 August 2004. The first two messages were neither acknowledged nor replied to as, in accordance with Article 14 of the Agency's Code, they were considered repetitive and pointless. A substantive reply to the complainant's e-mail of 23 August 2004 was nevertheless sent to the complainant on 5 October 2004, as soon as the agenda of the next CHMP plenary meeting was fixed. The outcome of the CHMP discussion of November 2004 was promptly reported to the complainant in a letter of 18 November 2004 from the Chairman of the CHMP.

The Agency concluded that it had acted in accordance with its Code as regards the deadlines for replies to queries received from the general public.

3.3 In her observations, the complainant stated that there had been a misunderstanding with regard to the Agency's reply of 19 January 2004.

As regards the Agency's argument that it did not answer the complainant's e-mails of 11 June 2004 and 6 July 2004 because they were abusive, the complainant considered this to be insulting, given that the relevant e-mails were necessarily repetitive due to the fact that her questions had not been answered. According to the complainant, Article 14 of the Agency's Code is merely a means to avoid having to answer questions.

3.4 The Ombudsman notes that, in this section of the decision, he will deal only with the allegation of undue delay and not with the substance of the replies which have been sent to the complainant. The substance of these replies forms the subject of the complainant's first and third allegations, which are dealt with in point 2 above and point 4 below.

3.5 As regards the alleged delay, the Ombudsman notes that the Agency's Code, which, subject to some minor differences, is the same as the European Code of Good Administration Behaviour, provides in Article 14 that:

" *[e]very letter or complaint to the Agency shall receive an acknowledgement of receipt within a period of two weeks, except if a substantive reply can be sent within that period (...). No acknowledgement of receipt and no reply need be sent in cases where letters or complaints are abusive because of their excessive number or because of their repetitive or pointless character.* "

3.6 The Ombudsman notes from the complaint and its annexes that, in the year 2004, the complainant sent a total of seven e-mails to the Agency, more particularly on 12 January, 27

May, 11 June, 6 July, 23 August, 26 November and 8 December 2004. The Ombudsman will therefore consider below how the Agency has reacted to each of these e-mails.

3.7 In her first, short, e-mail of *12 January 2004* to the Agency, the complainant asked for information on the Agency's review of Paroxetine/Seroxat or any relevant works regarding safety and the drug's suicide risk. The Ombudsman notes that Ms L. from the Agency's Document Management Sector replied to this e-mail on *19 January 2004* , that is, within seven days and, thus, within the two-week deadline foreseen in the Agency's Code. The Agency directed the complainant to its website, where all public documents were published.

3.8 On *27 May 2004* , the complainant sent a second e-mail to Mr T. from the Agency and asked for a copy of the full review, findings and recommendations of the Agency/CHMP on Paroxetine and for information on the review procedure, including the possibility for individuals to be heard in that context. The Ombudsman notes that the Head of Unit of Post-Authorisation Evaluation of Medicines for Human Use, Mr W., replied on behalf of the Agency to the complainant's e-mail on *11 June 2004* within the two-week deadline foreseen in its Code. The Ombudsman notes that, in her observations, the complainant wondered why the secretary of the then President of the European Parliament, Mr Pat Cox, whom the complainant had contacted in this matter, received a reply within a couple of hours, whilst she had to wait for 15 days. The Ombudsman notes that Mr Pat Cox's assistant, wrote to the Agency on 2 June 2004 at 15:28 (12) and received a reply the same day already at 17:32. On 3 June 2004, Mr Pat Cox's assistant forwarded the reply to the complainant. The Ombudsman notes however that the Agency's reply of 2 June 2004 was a holding reply (13) , whereas its reply to the complainant of 11 June 2004 was a substantive reply. The Ombudsman considers that this reasonably explains why the reply to Mr Cox's assistant was sent so quickly. As regards the substantive reply, the Ombudsman notes that Mr Cox's assistant was informed at the same time as the complainant, since the Agency's reply of 11 June 2004 to the complainant was copied to her.

3.9 On *11 June 2004* , the complainant wrote a third e-mail to the Agency replying to the latter's answer of the same day and asking several new questions. The Ombudsman notes that the complainant's e-mail remained both unacknowledged and unanswered within the two-week deadline foreseen in the Agency's Code.

3.10 On *6 July 2004* , the complainant wrote a fourth e-mail to the Agency, in which she stated that she was still waiting for a reply to her previous e-mail and a response to her questions, and that " *I would like a response please if it is not too much to ask* ". The Ombudsman notes that this e-mail also remained both unacknowledged and unanswered within the two-week deadline foreseen in the Agency's Code.

3.11 On *23 August 2004* , the complainant wrote a fifth e-mail to the Agency. The Ombudsman notes that this e-mail also remained both unacknowledged and unanswered within the two-week deadline foreseen in the Agency's Code. However, Mr W. replied on *5 October 2004* to the complainant's e-mail and provided further information and clarifications. On *18 November 2004* , the Agency, in the person of the Chairman of the CHMP, sent another letter to the complainant,

also in reply to her e-mail of 23 August 2004.

3.12 On *26 November 2004* and *8 December 2004* , the complainant sent a sixth and seventh e-mail to the Agency. These e-mails remained both unacknowledged and unanswered by the Agency.

3.13 On the basis of the above overview of the e-mail correspondence between the complainant and the Agency, the Ombudsman comes to the following findings with regard to the seven e-mails of the complainant:

3.14 The Ombudsman notes that, apart from the first two e-mails of the complainant of 12 January and 27 May 2004, which were answered by the Agency within the two-week deadline foreseen in its Code, five e-mails were either not answered or not answered within the two-week deadline.

3.15 As regards the complainant's two e-mails of *11 June* and *6 July 2004* , the Ombudsman has already come to the provisional conclusion, explained in point 2.14 above, that the failure to reply to them could constitute maladministration.

3.16 As regards the complainant's e-mail of *23 August 2004* , the Ombudsman notes that it remained initially unacknowledged and unanswered, but that the Agency finally replied to this e-mail on 5 October 2004 and also sent a further follow-up letter with the latest information on 18 November 2004. Although the two-week deadline was not respected with regard to the complainant's e-mail of 23 August 2004, the Ombudsman considers that, in view of the two replies which were sent by the Agency on 5 October and 18 November 2004, no further inquiries are necessary.

3.17 As regards the two e-mails of the complainant of *26 November* and *8 December 2004* which remained unanswered, the Ombudsman notes that both these e-mails were sent to the Agency for information. The e-mail of 26 November 2004 was very short, containing merely the sentence " *Dear sir/madam, Information for your records (...) Yours sincerely* " and three links to the US Food and Drug Administration's website (http://www.fda.gov [Link]). The e-mail of *8 December 2004* was sent to the Agency and at the same time to three Irish e-mail addresses. This e-mail, which had as subject title " *Fw: SSRIs* ", contained an attachment and a forwarded message, which read " *For your information. Not all the risk-benefit profiles are positive on the SSRIs. On mild depression the risk-benefit is POOR* ". Considering that it appears from the text itself of these e-mails that they were clearly for information only, the Ombudsman considers that the fact that the Agency did not reply to these e-mails does not constitute an instance of maladministration.

4 The allegation that the complainant was not heard and that there was a lack of action by the Agency with regard to her concerns

4.1 The complainant alleged that she was not heard by the Agency with regard to the matter of the safety and suicide risks of Paroxetine and that her opinion was not taken into account. She further alleged that there was a lack of action by the Agency regarding her concerns. As regards the latter, the complainant expressed serious concerns in her complaint about the Agency's

failure to protect the public (page 5 of the complaint). She also stated that she expected the Agency to work properly and that this meant that it should protect her and her family from well-known drug-induced harm (page 7). In the complaint form, the complainant also referred to the lack of appropriate warnings as regards preventable harm.

4.2 In its opinion, the Agency pointed out that the relevant legal provisions of the pharmaceutical legislation do not grant individuals the right to be heard in the framework of the assessment procedure. The representatives of the CHMP and the Agency had nevertheless heard the scientific concerns expressed by a group of user patients as distinct from a single individual and the CHMP had also agreed to a follow-up letter sent on 18 November 2004 by the CHMP Chairman to the complainant. The Agency also stated that it acted in accordance with the provisions set out in the relevant applicable legislation and in its Code.

4.3 In her observations, the complainant observed that the Agency/CHMP had heard scientific concerns expressed by a group of Seroxat User patients. The complainant included with her observations two reports of the meeting held at the Agency on 19 April 2004. During the meeting, the Agency made it clear that it was not standard practice to listen to patients' scientific concerns. According to the complainant, this meeting was merely an attempt to attract publicity. The complainant observed that the review was completed and a press release was issued on 22 April 2004, merely three days after the meeting with the Seroxat User Group about their scientific concerns. According to the complainant, this indicates that it was never CHMP's intention to pay any attention to what the Seroxat User Group had to say. The complainant emphasised that there is something fundamentally wrong if the Agency does not have a responsibility to listen to the individuals who are the clinical experts in the field. However, the Agency appears to listen to pharmaceutical companies.

4.4 The Ombudsman notes that the complainant's observations refer to the hearing of other persons/bodies, namely, the Seroxat User Group. Given that the original complaint only concerned the alleged failure to hear the complainant herself, the Ombudsman considers that the reference to the hearing of other persons does not appear to constitute a new allegation, but rather a comment made in the framework of the original complaint.

4.5 The Ombudsman notes that the complainant's allegation that she was not heard with regard to the matter of safety and the suicide risks of Paroxetine has to be considered from the point of view of the procedure foreseen for the adoption of medicine marketing authorisations. In this regard, the Ombudsman notes that the CHMP is responsible for preparing the Agency's opinions on all questions concerning the evaluation of medicinal products for human use. The relevant procedure in this regard is described in Directive 2001/83/EC on the Community Code relating to medicinal products for human use (14) ("Directive 2001/83") . Following the opinions prepared by the Agency, it is however the Commission which takes the final decision on the marketing authorisation (15) .

4.6 In the present case, the procedure which was followed with regard to medicines containing Paroxetine was the referral procedure (Articles 31 to 34 of Directive 2001/83), which was initiated by the MHRA under Article 31 of the Directive. The MHRA launched the procedure as a

result of safety concerns relating to potential risk of emotional changes, such as crying, mood fluctuations, hostility, self-harm, suicidal thoughts as well as attempted suicide, and withdrawal reactions associated with the use of Paroxetine.

4.7 The Ombudsman notes that the CHMP's Rules of Procedure (16) do not foresee the possibility for an individual patient or his/her representative to be heard, but provide for " *[c]ontacts with interested parties* " in Article 23(1) which foresees that

" *[t]he Committee (...) will establish contacts, on an advisory basis, with parties concerned with the use of medicinal products,* in particular patient organisations *and health-care professionals' associations. The Committee may agree to invite representatives of such interested parties to address a plenary meeting* " (emphasis added).

Article 23(3) provides that " *[w]hen considered appropriate by the Committee, oral presentations by interested parties can be made during working party or scientific advisory group meetings in earlier stages of development of guidelines. The working parties may also meet with interested parties to discuss general matters or specific scientific issues with the agreement of the Committee and under specific conditions to be agreed by the Committee* ".

4.8 It appears that, as regards the review of the benefits and risks of medicines containing Paroxetine, the CHMP indeed organised a meeting on 19 April 2004 with representatives from a group of patients, namely, the Seroxat User Group. The Ombudsman notes from the two reports of this meeting which the complainant attached to her observations that the members of the Seroxat User Group (17) were given the possibility to describe their personal experiences concerning the undesirable effects of treatment with Paroxetine. They were heard by the Chairman and several other members of the CHMP. The Ombudsman notes more particularly that several members from the Seroxat User Group present at the meeting described experiences of suicide attempts.

4.9 The Committee finally adopted its opinion at its meeting of 22 April 2004. In its opinion, the Committee concluded that the risk-benefit assessment for medicines containing Paroxetine remained positive, but made several recommendations. The Ombudsman notes that, in its reply of 11 June 2004 to the complainant's e-mail of 27 May 2004, the Agency informed the complainant about these developments and about the meeting with the Seroxat User Group.

4.10 Although the procedure in question does not provide for a right of an individual patient or his/her representative to be heard, the Ombudsman notes that the CHMP Rules of Procedure appear to leave a discretionary power to the CHMP to obtain views from interested parties. In the present case, it appears that the Agency, in its reply of 5 October 2004 to the complainant's e-mail of 23 August 2004, informed the complainant that her questions concerning the suicide warning had been brought to the attention of the CHMP. The CHMP appears thus to have considered the complainant's arguments. The Ombudsman considers that the complainant has not established that the CHMP would have been obliged to hear her in person.

4.11 On the basis of the above considerations, the Ombudsman concludes that, although it did

not hear the complainant personally, the Agency consulted the Seroxat User Group and has also taken account of the complainant's concerns. Considering furthermore that it appears that the Agency has acted in accordance with the applicable procedures, the Ombudsman found no instance of maladministration by the Agency with regard to the complainant's allegation that she was not heard.

4.12 As regards the complainant's allegation that there was a lack of action by the Agency with regard to her concerns, the Ombudsman notes that, by "lack of action", the complainant was in fact referring to the alleged failure of the Agency to protect the public from drug-induced harm and to provide appropriate warnings. The complainant appears thus to object to the outcome of the review by the Agency of medicines containing Paroxetine, particularly as regards the warnings contained in the product description. The complainant mentioned in this context that GSK had been required in Canada and the United States to implement more explicit warnings about the same drug (cf. her e-mail of 11 June 2004).

4.13 The Ombudsman notes that the CHMP reaffirmed the conclusion it had reached in its opinion of 22 April 2004 that the risk-benefit assessment remained positive for medicines containing Paroxetine used in the treatment of adults and that it confirmed the previously recommended changes to the product information for Paroxetine on an EU-wide basis (18) .

4.14 The Ombudsman notes that the Agency is the expert EU body in the field of medicines. The Ombudsman does not have the necessary specialised expertise in the field concerned and thus cannot (and should not) substitute his own views for those of the Agency. The Ombudsman's role is to examine whether there has been maladministration. In the present case this means, in view of the above, that he should examine whether the Agency has taken into account all relevant information and whether it has made a manifest error as regards the assessment of these facts.

4.15 The Ombudsman notes that, according to the Agency's website, a ssessments conducted by the CHMP are based on purely scientific criteria and determine whether or not the products concerned meet the necessary quality, safety and efficacy requirements, in accordance with EU legislation, particularly Directive 2001/83. These assessments are intended to ensure that, once they are put on the market, medicinal products have a positive risk-benefit balance in favour of patients/users of these products. The Ombudsman considers that in order to fulfil this task, the Agency needs to take into account all relevant facts. In the present case, the Ombudsman notes that, in its reply of 11 June 2004 to the complainant, the Agency pointed out that the CHMP had considered the available data on suicide, suicide attempts, suicidal ideation from clinical trials, as well as data derived from spontaneous reports and the published literature. It also heard a group of Paroxetine users. The Ombudsman notes that several participants in the meeting with Paroxetine users referred to suicide attempts or suicides by close relatives. In its reply to the complainant, the Agency also stated that it encourages the reporting, at the EU level, of suspected serious adverse effects of medicines, including Paroxetine. The Agency added that each reported case is evaluated, taking into account the clinical view of the attending physician who is most familiar with the medical condition of the patient concerned. For more information about the reporting system, the Agency referred the complainant to the Irish

Medicines Board. Given that the complainant had informed the Agency of her husband's suicide and of her view that this suicide was caused by the relevant drug, the CHMP would thus appear to have taken its decision on the review of medicines containing Paroxetine in full knowledge of these facts.

4.16 With regard to the complainant's argument that more explicit warnings apply in the United States and Canada with respect to medicines containing Paroxetine, the Ombudsman notes that, in its opinion (pages 7-8) on complaint 2371/2005/OV, the Commission submitted that this argument was not correct. According to the Commission, the content of the information regarding Paroxetine and the risk of suicide/suicide behaviour is the same in all the countries concerned, and the only difference is to be found in the way in which this information is presented. For instance, it is common practice in the United States to include such information in so-called black boxes. This method is not available in the EU in a harmonised manner due to the different implementation of medicinal product legislation at the national level. Also, European legislation does not require that certain information/warnings have to be presented in a specifically "eye catching" way, like the "black box warning" in the United States or Canada. The Ombudsman notes that, in her observations on the Commission's opinion in case 2371/2005/OV, the complainant rejected this argument. She referred to several extracts from the warnings of the US Food and Drug Administration (FDA) of 22 March 2004 which, in her view, were more explicit than the relevant EU warnings (19) . The complainant made the same remarks with regard to warnings in Canada. The complainant suggested that the Ombudsman compare the wording and contents of the above-mentioned warnings. As stated in point 4.14 above, the Ombudsman would like to recall that he does not have the necessary expertise to compare the level of the warnings between, on the one hand, the EU and, on the other hand, the United States and Canada. The Ombudsman also recalls that the Agency is the EU's specialised body in this field. The Ombudsman considers, however, that the Agency would appear to have taken into account the complainant's argument when reaching its decision on the review of Paroxetine.

4.17 The Ombudsman furthermore considers that the complainant has not established that the Agency and/or the CHMP committed a manifest error as regards the assessment of the relevant facts. It is clear from the complaint and the complainant's observations that she is not satisfied with the outcome of the Agency's review of medicines containing Paroxetine and with its final opinion. The Ombudsman would like to point out however that it is the essence of a decision-making process that there will always be different views as regards the merits of the final decision adopted. However, this does not mean that there has been maladministration in the adoption of the decision.

The possibility of a friendly solution

Article 3(5) of his Statute directs the Ombudsman to seek, as far as possible, a solution with the institution concerned to eliminate the instance of maladministration and satisfy the complainant.

With regard to the complainants' allegations of lack of information and undue delay, the Ombudsman therefore made the following proposal for a friendly solution to the Agency:

The Agency could consider (i) apologising to the complainant for having referred to her e-mails

of 11 June and 6 July 2004 as being repetitive and pointless and (ii) replying to the questions raised by the complainant in these e-mails.

The Agency's reply to the Ombudsman's proposal

The Agency stated that it accepted the Ombudsman's proposal for a friendly solution and apologised to the complainant for neither having acknowledged nor replied to her e-mails of 11 June and 6 July 2004 and for unintentionally having caused her distress during an extremely difficult time in her life.

The Agency also wanted to clarify that, even if these e-mails were different in nature from the one sent by the complainant on 27 May 2004, the essence of the questions was already covered by its reply of 11 June 2004. In this reply, the Agency provided the complainant with all information which could be released at the time and explained in detail the procedure which would be followed for the adoption of the Commission Decision.

In retrospect, as it became clear that the complainant did not consider the questions adequately addressed in the Agency's replies of 11 June and 5 October 2004, the Agency also wanted to apologise for describing the complainant's repeated e-mails as pointless. The Agency concluded that, for the above reasons, it was willing to answer the questions raised by the complainant in her e-mails of 11 June and 6 July 2004.

The Agency enclosed with its reply the answer it had sent to the complainant on 1 October 2007. This letter contained the above explanations, followed by replies to the following three questions of the complainant " *Did CHMP request all data from all clinical trials held by GSK before drawing their opinion for the adult population? Has the Commission prepared a draft of the decision to be taken yet? Has any Member State raised important new questions of a scientific or technical nature which have not been addressed in the opinion of the EMEA/CHMP? How do you explain the difference on warnings of the same drug in the USA/Canada/EU?* "

The complainant's observations

In her e-mail of 2 October 2007 to the Ombudsman, the complainant pointed out that the Agency's reply to her of 1 October 2007 was disheartening. The complainant wondered whether the Agency had read the Ombudsman's findings at all. The complainant found the letter patronising and stated that it read like " *we are apologising because we have to, but we are not wrong* ". The apology was meaningless according to the complainant.

The complainant stated that, once again, her main question " *Did CHMP request all data from all clinical trials held by GSK before drawing their opinion for the adult population?* " had not been answered. The complainant stated that there are only two possible answers to this question: yes or no. The complainant concluded that she did not accept the meaningless apology letter as a settlement of the findings of maladministration contained in the Ombudsman's letter of 26 July 2007 to the Agency.

In a telephone conversation with the Ombudsman's Office on 3 October 2007, the complainant reiterated that the Agency letter to her of 1 October 2007 was not a sincere and meaningful apology.

In another telephone conversation with the Ombudsman's Office on 13 November 2007, the complainant indicated that she would not submit further observations and that her e-mail of 2 October 2007 to the Ombudsman constituted her observations on the Agency's reply to the proposal for a friendly solution.

THE DECISION

1 The alleged lack of transparency and lack of information, the alleged undue delay and the allegation that the complainant was not heard and that there was lack of action by the Agency

1.1 The complainant is an emergency nurse in Cork University Hospital. On 26 December 2003, and at the age of 39 years, the complainant's husband and father of her three children, committed suicide while taking Seroxat (20) /Paroxetine, an anti-depressant. According to the complainant, Seroxat caused her husband to commit suicide. After the death of her husband, the complainant therefore contacted the European Medicines Agency (hereafter "the Agency") with regard to the use, the dangers and warnings of Selective Serotonin Reuptake Inhibitors ("SSRIs") and Paroxetine in particular. The complainant in particular requested information regarding the Agency's scientific opinion on Paroxetine and any other information regarding the drug's safety and suicide risk. The complainant was however not satisfied with the response to her e-mails received from the Agency. In her complaint to the Ombudsman, the complainant made the following three allegations: 1) there has been a lack of transparency and information by the Agency and its CHMP (21) with regard to her request for their review on Paroxetine and any other information regarding the safety and suicide risk of the SSRIs and Paroxetine in particular; 2) there has been undue delay in the replies to her e-mail correspondence; 3) the complainant was not heard by the Agency with regard to the matter of the safety and suicide risks of Paroxetine and her opinion was not taken into account. Also, there was a lack of action by the Agency regarding her concerns.

1.2 On the basis of his analysis of the file in his proposal for a friendly solution of 26 July 2007, the Ombudsman found no instance of maladministration with regard to the complainant's third allegation.

1.3 With regard to the first and second allegations of lack of information and undue delay, the Ombudsman on 26 July 2007 addressed a proposal for a friendly solution to the Agency, suggesting that it could consider (i) apologising to the complainant for having referred to her e-mails of 11 June and 6 July 2004 as being repetitive and pointless and (ii) replying to the questions raised by the complainant in these e-mails.

1.4 In its reply of 1 October 2007, the Agency stated that it accepted the Ombudsman's proposal for a friendly solution. The Agency apologised to the complainant for neither having acknowledged nor replied to her e-mails of 11 June and 6 July 2004 and for unintentionally having caused her distress during an extremely difficult time in her life. The Agency also apologised for having described the complainant's repeated e-mails as pointless. The Agency enclosed with its reply the answer it had sent to the complainant on 1 October 2007. This letter contained the above explanations, followed by replies to the following three questions of the

complainant " *Did CHMP request all data from all clinical trials held by GSK* [GlaxoSmithKline] *before drawing their opinion for the adult population? Has the Commission prepared a draft of the decision to be taken yet? Has any Member State raised important new questions of a scientific or technical nature which have not been addressed in the opinion of the EMEA* (22) */CHMP? How do you explain the difference on warnings of the same drug in the USA/Canada/EU?* "

1.5 In her observations, the complainant stated that the Agency's reply of 1 October 2007 was disheartening. The complainant wondered whether the Agency had read the Ombudsman's findings at all. The complainant found the letter patronising and stated that it read like " *we are apologising because we have to, but we are not wrong* ". The complainant stated that, once again, her main question, namely " *Did CHMP request all data from all clinical trials held by GSK before drawing their opinion for the adult population?* " had not been answered. The complainant concluded that she did not accept the meaningless apology letter as a settlement of the findings of maladministration contained in the Ombudsman's letter of 26 July 2007 to the Agency.

1.6 The Ombudsman notes that the Agency has accepted his proposal for a friendly solution. The Ombudsman notes in particular that, in both its reply to the Ombudsman and in its letter of 1 October 2007 to the complainant, the Agency has apologised to the complainant for not having replied to her e-mails of 11 June and 6 July 2004 and for having described her repeated e-mails as pointless. In the Ombudsman's view, there is nothing to suggest that the Agency's apology was insincere. The Ombudsman further notes that in its letter to the complainant of 1 October 2007, the Agency replied to the questions raised by the complainant in these e-mails.

1.7 With regard to the question " *Did CHMP request all data from all clinical trials held by GSK before drawing their opinion for the adult population?* ", the reply to which the complainant found unsatisfactory, the Ombudsman notes that the Agency replied the following to the complainant: " *(...) In fact as part of the review the CHMP requested all Marketing Authorisation Holders* [MAHs] *for paroxetine containing medicinal products in the European Union, including GSK, to provide 'All data relating to the risk of self-harm, hostility and suicidal behaviour with paroxetine from all data sources including clinical trials, spontaneous reporting, observational studies, healthy volunteer studies and consumer reports' (CHMP List of Questions, CPMP/16519/03 of 26 June 2003). In addition, the CHMP asked the MAHs to 'provide the narratives of the case reports for the suicide that occurred during clinical trials' (CHMP List of Outstanding Issues, CPMP/5759/03 of 20 November 2003)* ". The Ombudsman considers that this reply would appear to address the question that had been put to the Agency by the complainant. The same conclusion applies to the Agency's replies to the complainant's two other questions.

1.8 The Ombudsman very much welcomes the fact that the Agency has accepted his proposal for a friendly solution. However, given the fact that the complainant has made it clear that she remains dissatisfied the Ombudsman concludes that no friendly solution could be achieved in the present case. The Ombudsman nevertheless notes that the Agency has addressed the issues that he considered to constitute possible instances of maladministration. He further

considers that the action taken by the Agency was sufficient to remove his concerns. The Ombudsman therefore takes the view that, bearing in mind the letter addressed to the complainant by the Agency on 1 October 2007, there is no longer any maladministration on the part of the Agency.

2 Conclusion

The Ombudsman concludes that there is no longer any maladministration on the part of the Agency. The Ombudsman therefore closes the case.

The Ombudsman would finally like to sincerely express his regret for the fact that he cannot be of further assistance to the complainant. As already pointed out when he made his proposal for a friendly solution on 26 July 2007, the Ombudsman realises that the complainant has gone through an extremely difficult time in her life due to the suicide of her husband. The Ombudsman also realises that the assistance he could provide to the complainant in the framework of the present inquiry was very marginal in comparison to the tragedy she suffered. The Ombudsman would however like to reiterate to the complainant his deepest sympathy for her loss and his kind wishes for her future and that of her family.

The Executive Director of the European Medicines Agency and Mr Brian Crowley MEP will also be informed of this decision.

Yours sincerely,

P. Nikiforos DIAMANDOUROS

(1) Seroxat is a medicine containing Paroxetine.

(2) " *Every letter or complaint to the Agency shall receive an acknowledgement of receipt within a period of two weeks, except if a substantive reply can be sent within that period. (...)*

No acknowledgement of receipt and no reply need be sent in cases where letters or complaints are abusive because of their excessive number or because of their repetitive or pointless character. "

(3) Doc. Ref. EMEA/6470/03/2368.

(4) This CHMP was formerly called the Committee for Proprietary Medicinal Products ("CPMP"). As the Committee's last meeting under its former name was held on 22 April 2004, and as the Agency afterwards exclusively referred to it in its opinion as "CHMP", the present decision refers only to the current name.

(5) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, OJ 2001 L 311, p. 67.

(6) The Ombudsman notes that these two reports were prepared by the Seroxat User Group (http://www.seroxatusergroup.org.uk [Link]).

(7) The complainant also submitted a complaint against the Commission (2371/2005/OV) concerning the same subject-matter as the present case. The Ombudsman's inquiries into this case are ongoing.

(8) See, more particularly, point 9 of the "New EMEA transparency policy measures" (EMEA/MB/52/03/Rev 1/Final, London, 31 October 2003), which is available on EMEA's website (http://www.emea.europa.eu/pdfs/general/manage/mbar/Transparancy%20pol/005203en.pdf [Link]).

(9) There was a warning to reflect the fact that Paroxetine should not be used in children and adolescents, given that data from clinical trials raised concerns regarding suicidal behaviour and hostility. There was also a warning to prescribers which recommended the close monitoring of patients at high risk of suicidal behaviour, including patients with a known history of suicidal behaviour or of suicidal thoughts prior to starting treatment, and possibly young adults.

(10) Decision on rules on access to EMEA documents, 7 October 2004, EMEA/MB/67083/2004.

(11) Commission Decision of 29 March 2005 concerning the placing on the market, under Article 31 of Directive 2001/83/EC of the European Parliament and of the Council, of the medicinal products for human use which contain the active substance "Paroxetine".

(12) The Ombudsman notes that, in her e-mail of 2 June 2004, Mr Pat Cox's assistant referred to the complainant's situation, stated that she would appreciate any assistance and advice the Agency could offer to the complainant, and asked the Agency if it could outline the procedure concerning the review of Paroxetine.

(13) The reply stated that the e-mail had been forwarded for reply to the Head of Unit who would contact Mr Pat Cox's assistant in the following days.

(14) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use, as amended, OJ 2004 L 311, p. 67.

(15) See Article 34 of Directive 2001/83/EC.

(16) The Rules of Procedure are available on the CHMP's website (http://www.emea.europa.eu/htms/general/contacts/CHMP/CHMP.html [Link]).

(17) The persons present were from the Seroxat User Group, and other bodies such as "OSSG", "APRIL" and "MIND". The Agency was represented by the Chairman of the CHMP and five other persons.

(18) " *The changes included:*

- A warning to reflect that Paroxetine should not be used in children and adolescents. In the EU Paroxetine is not authorised for use in this population. Data from clinical trials raised concerns regarding suicidal behaviour and hostility. In addition, data from clinical trials have not adequately demonstrated efficacy in these age groups.

- A warning to prescribers recommending close monitoring of patients at high risk of suicidal behaviour. These include patients with a known history of suicidal behaviour or suicidal thoughts prior to starting treatment, and possibly also young adults.

- Prescribers and patients should be warned regarding the occurrence of withdrawal reactions upon stopping treatment. Generally these are mild to moderate and self-limiting. However, in some patients they may be severe and/or prolonged ".

(19) The Ombudsman notes that the summary of product characteristics for Paroxetine in the EU contains the following warning under the title "Special warnings and Special Precaution for use":

" *Suicide/suicidal*

Depression is associated with an increased risk of suicidal thoughts, self harm and suicide. This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience with all antidepressant therapies that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which Paroxetine is prescribed can also be associated with an increased risk of suicidal behaviour. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.

Patients with a history of suicidal behaviour of thoughts, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are at a greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment (...). "

(20) Seroxat is a medicine containing Paroxetine.

(21) Committee for Medicinal Products for Human Use.

(22) EMEA stands for the Medicines Agency.