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Copies to :

- Eric Abadie, Committee for Medicinal Products for Human Use, EMA
- Jean Marimbert, Executive Director, Afssaps
- Markos Kyprianou, European Commissioner (Health)
- Günter Verheugen, European Commissioner (Vice President Enterprise and Industry)

Dear Mr Lönngren,

As a coalition of eight French HIV/AIDS NGO's (Act Up-Paris, Actions Traitements, AIDES, Arcat, Dessine Moi Un Mouton, Nova Dona, Sida Info Service, Sol En Si), the main objective of TRT-5 is to advocate for the medical and research needs of people living with HIV.

The recent detection, in some batches of Viracept® (manufactured in Europe by Roche), of a known genotoxic substance, potentially carcinogenic and teratogenic in humans (EMS for ethyl mesilate), leads us to ask you some important questions regarding the quality of drugs authorized by EMA.

I – Guarantee of quality and security, transparency on the checks planned before and after the marketing authorization of a medicinal product

Viracept® was recalled from the European market on 6 June 2007, following some complaints of patients disturbed by a bad smell or suffering from nausea. Further analysis showed that recent batches of nelfinavir mesilate (from March 2007) were contaminated with high levels of ethyl mesilate, but also that EMS was present (at a lower level) in some batches released during the previous years. However, as you may know, substances that can lead to the formation of alkyl mesilates are commonly used in manufacturing processes of medicinal products. So the risk of contamination by EMS was perfectly foreseeable and known.



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How then can one explain this late detection ? Are EMS levels in Viracept batches regularly measured ? More generally, what are the scheduled procedures, in compliance with good manufacturing practices, for the quality control of medicinal products authorized by EMEA ? Are sample analyses routinely performed or is quality assurance only based on manufacturing and testing records ?

We want to know precisely what checks have been performed on Viracept since the first use of this drug in humans. As we strongly need to understand what really happened, we would like to have access to the full report established by toxicology experts appointed by EMEA to investigate Roche's manufacturing sites.

We do not accept that such a crisis could happen again. Therefore we ask EMEA to organize a consultation on good manufacturing practices and inspections for all medicinal products. And we want the specific question of the detection of contaminants to be addressed by EMEA experts, in order to ensure complete safety for the patients.

As you may know, adherence to treatment is crucial for all patients suffering from HIV. This adherence is linked to numerous factors ; one of them is the confidence that patients do have in the safety of the medicinal products prescribed. This crisis generates a loss of confidence and discredit regarding the quality of medicinal products in HIV, and of medicinal products in general. As you can imagine, the lack of clear and precise information from Roche and EMEA increases each day our worries for the patients exposed to contaminated Viracept®.

II - Action plan to follow-up patients - Communication to patients

The Agency's Committee for Medicinal Products for Human Use (CHMP) has asked the company to follow patients exposed to high levels of contaminant in the batches of Viracept released since March 2007, all pregnant women who have ever been exposed to Viracept and all children who have ever been exposed to Viracept, including those exposed *in utero*. But more than 40 days after the alert, Roche has given absolutely no details about its action plan. In this situation, we consider this incomplete communication might cause a lot of anxiety in the patients exposed.

Moreover we are surprised by the fact that EMEA publishes such a press release on its website (1), without taking into account the time needed by national agencies to adapt the message to their local specificities.

And this leads us to a strange configuration : EMEA communicates early but incompletely, and patients have to wait for several days to know exactly what they should do and expect from us. We think, and suggest that communication to the patients and the general public, in such a crisis situation, can be improved.

III - Problems linked to the replacement of Viracept

While EMEA and Roche communicate on action plan to follow-up patients, nothing is said to address the responsibilities of the recall. In particular, nothing is publicly asked to Roche concerning the replacement of Viracept®.

However, in France, and surely in many other European countries, some rare patients are not easily switched to another HIV medication (ARVs). We are really surprised that, to this day, no import have been anticipated nor planned for the few patients concerned. What is the explanation for this lack of anticipation ? Has EMEA established some contacts with the FDA to ease a possible access to the Viracept® product manufactured by Pfizer ?

When we ask our local counterparts about the situation in Africa, we hear that people lack crucial information in the countries concerned. Patients are not proactively informed about the recall of

Viracept® : in the best case, they are switched by their doctors at the next visit. Unfortunately, as you may know, there are not always any alternative drugs to replace Viracept®, or they are unaffordable, or not indicated for a given patient. Moreover, as a consequence, the recall of Viracept® depletes the stocks of drugs available, and deprives some patients of the ARV treatments they crucially need.

Africa suffers in an unbearable way from the lack of ARVs and from weak healthcare infrastructures; this continent should not suffer also from the severe deficiencies of pharmaceutical firms.

We deplore that the Health authorities have not, until now, given strong directives to Roche : in our point of view, Roche must compensate for all the types of difficulties linked to the recall of Viracept® and, precisely, Roche must provide free access to ARVs wherever necessary.

To conclude, we want the responsibilities of each actor to be clearly established. Also we do not accept that any patient, living in the North or in the South, would suffer from the consequences of this crisis.

We hope that all the answers to the questions raised, concerning the potential toxicity of EMS, the cause of the contamination, and the compensation offered to patients exposed, will be given soon and with total transparency.

You will understand that we shall follow with acute attention any new development regarding this affair. We will be vigilant, because we do not want such a crisis to happen again.

Looking forward to your prompt reply,

Yours sincerely.

For TRT-5 and for the organisations members of TRT-5,

Bruno Spire, AIDES Chairman



Anne Guérin, Arcat Director

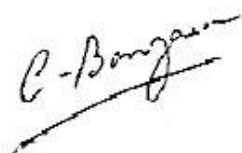
Jean-Marc Bithoun, Actions Traitements Chairman



Emmanuel Château et Hugues Fisher, Act Up-Paris Co-Chairmans



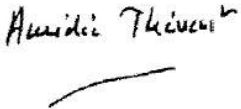
Claire Bougaran, Dessine Moi Un Mouton Chairwoman



Vanessa Dubus-Bonnet, Sol En Si Chairwoman



Amédée Thévenet, Sida Info Service Chairman



Corinne Taéron (2), TRT-5



(1) <http://www.emea.europa.eu>