

Mr. Franz Humer
CEO, Roche Laboratories

Paris, le 20 July, 2007

Dear Mr. Humer,

As a coalition of eight French HIV/AIDS NGOs (Act Up-Paris, Actions Traitements, AIDES, Arcat, Dessine Moi Un Mouton, Nova Dona, Sida Info Service, Sol En Si), the main purpose of TRT-5 is to lobby for the needs and rights of people living with HIV to actors involved in research and care, institutions and the pharmaceutical industry.

In this capacity, we are concerned by a certain number of questions following the recent detection in Europe and France of batches of Viracept[®] contaminated by a potentially carcinogenic and mutagenic genotoxic substance in humans, ethyl mesilate (EMS).

To date, information given out by Roche about this contamination has been slow in coming and vague. Nor have we seen any substantive measures from your laboratory to make up for the harm done to the patients who have taken or are still taking this treatment. All of which only increases our concerns for these people and raises intolerable doubts about the manufacture of all your products.

We are asking you as manufacturer, patent-holder and responsible for Viracept[®] in Europe and several other of the world's regions to provide us with detailed answers to our questions, which are listed in the annex to this letter and which we would ask you to consider as an integral part of it.

The residual presence of EMS in the manufacturing process of Viracept[®] is known. Moreover the use of alkyl mesilates seems common to the manufacture of numerous drugs. Yet according to our information, the alarm was sounded not in the wake of detecting the problem by your monitoring services

TRT 5

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but by patients complaining of the drug's smell or of nausea. How is it that in your laboratories there is no strict surveillance of the presence of EMS in the batches and of real and known risk of exceeding authorised quantities? What verifications were carried out when the various authorisations for using Viracept® were applied for? This question concerns all the products involved in the manufacturing process of the drug, i.e. are we to understand that you only test for the presence of the active ingredient and the excipients of the batches to be released?

According to our information⁽¹⁾, although the problem appears to have taken on a particular dimension in March, 2007, it could well go back considerably farther in time. We are stunned to note that although the recall of batches took effect over a month ago, your services have been as yet unable to provide all the details about the extent of this contamination.

At present you tell us that the contamination-related risk is impossible to determine. Additional tests are underway. We have also learned that patients may be monitored. In case of avowed or suspected risk, what are Roche's commitments in relation to the people involved?

Moreover it appears that in France and probably in other European countries certain patients might have a hard time changing medication. It would have made sense to suggest making nelfinavir made by another laboratory (Pfizer or Cipla) available, i.e. how can you explain that agreements with these companies were not reached? When we query your services, we receive only vague answers. What efforts have you made to make imports possible?

And finally we are hearing worrying reports from African countries. Information there is being minimally distributed if at all. And that patients in numerous places are simply not informed about the Viracept® recall. Concordant accounts reveal that changing the drug only occurs when the prescription of the treatment is renewed each month. The substitution offered for the Viracept® is for drugs that are sometimes unavailable or poorly adapted. Moreover this improvised substitution disorganises already limited stocks of drugs and deprives other patients of treatment. Patients potentially find themselves in a situation of therapeutic failure, if not completely without treatment whilst they are in cruel need of them. Despite the fact that the African continent is already suffering intolerably from the lack of treatments and care, it appears that no support logistics for facilitating the recall and managing the consequences (making replacement antiretrovirals available free of charge) has been materially undertaken or even encouraged by your laboratory.

What therefore has Roche undertaken for all the patients living in poor countries that have been seriously compromised by your actions?

Mr. Humer, we are asking Roche in the most urgent terms to gauge the extent of your responsibility and to at last provide correct and exhaustive information about the problems encountered. We are asking you to provide adequate measures to all the victims of the your company's carelessness in order to care for them and ensure long-term monitoring of them as well as compensation for the damage done. Otherwise we can do little else than come to the conclusion that your consideration and mobilisation are insufficient.

In the hopes of a prompt reply to this letter, we, TRT-5 and its associate members, are yours sincerely,

Bruno Spire, President, AIDES



Anne Guérin, Director, Arcat

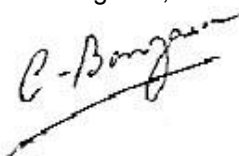
Jean-Marc Bithoun, President, Actions Traitements



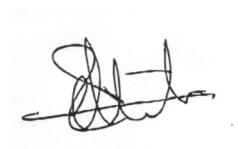
Emmanuel Château and Hugues Fisher, Co-Presidents, Act Up-Paris



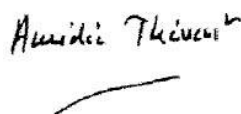
Claire Bougaran, President, Dessine Moi Un Mouton



Vanessa Dubus-Bonnet, President, Sol En Si



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Corinne Taéron⁽²⁾, for TRT-5



⁽¹⁾ <http://www.emea.europa.eu>

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cc: Eric Abadie, President, CHMP of EMEA
Jean Marimbert, Director, AFSSAPS

ANNEX: Question list

About the contamination and quality controls:

- What are the usual quality-control procedures for production in your laboratories?
- Is not the detection of organoleptic defects such as smell, looks and colours scheduled prior to batch release?
- Have you drawn up a list of the contaminated batches? What are their shipping dates and their code numbers? What proportion do they represent out of all the batches produced?
- What are the quantities of EMS found by monitoring the various incriminated batches (maximum quantity per tablet/average quantity per tablet from the same monthly treatment bottle)?
- Are you able to track the contaminated batches?
- What about Invirase®? Does the manufacturing process also contain alkyl mesitates? If so, what controls did you do? Is there a risk of the contamination recurring?
- The presence of EMS is tolerated at under 1 ppm in your manufacturing process. Did you specify the presence and the quantity when the pre-market approval and NDA requests were made? How old is the latest definition of presence and quantity, done during routine quality tests prior to releasing Viracept® batches? How many contamination-research-per-sub-standard doses of EMS were planned by your fabrication standards and at what intervals? How many of them were carried out? Were they just paper checks or were batch analyses done? At what intervals? And dates?

About EMS:

- Certain press releases have mentioned carcinogenic, mutagenic and teratogenic effects. Where do we stand?
- Tests have been done on rats. Can you indicate the precise types of tests done (absorbed dose, how administered, the number of animals involved, etc.)? What were the exact effects observed? With what frequencies? Were the effects noted only EMS-related or in synergy with other molecules? After how many administrations did they appear? Were these effects dose-dependent?
- How many tests and on what kinds of animals—including gestating females, newborn and young animals—are you going to do, and when do you intend to make the results available?
- What do you know about the stability of EMS? Do the detected quantities in later analyses correspond to the quantities absorbed by patients?

About your commitments to patients:

- A statement made last June 22nd by Mr. William Burns mentioned the follow-up of patients who have taken this treatment. Can you specify the way in which you register these people as well as the kind of the follow-up they received? What commitments have you made to them?
- Concerning patients not able, for whatever reason, to use other protease inhibitors than nelfinavir, do you plan to supply this Pfizer- or Cipla-made treatment free of charge?
- What do you intend to do about the possible resumption of the production of Viracept® in your laboratories?
- In the southern countries, especially in Africa, what are you planning to do for people to be correctly informed and able to benefit free of charge from a real adapted change of medication as fast as possible?
- What compensation are you planning for the victims?