Monsieur FISCHER, Président. - Merci beaucoup.

<u>Audition 14 : Pr Heidi J.LARSON, London School of Hygiene & Tropical Medicine (LSHTM)</u>

Madame LARSON – Hi, It's Heidi LARSON calling in.

Monsieur FISCHER, Président. – This is Alain FISCHER speaking.

Madame LARSON – Hello. I would try to get into the computer, but it got to a certain point and I could try the phone.

Monsieur FISCHER, Président. – The phone is working anyway, and I think that everyone is hearing you pretty well. Thank you very much for being with us. It would be ideal to also get your slides. Can you send the slides by email, please ?

Madame LARSON – Yes, I'll do that now to the group.

Monsieur FISCHER, Président. – Thank you very much. Take your time. Don't worry.

Madame LARSON – Thank you. Okay.

De 1:58 à 2:03, les participants règlent des détails techniques pour la retransmission.

Monsieur FISCHER, Président. – Just to give you a few words of introduction to tell you in which context we asked you to talk to us, we are a comity of approximately fifty people. There are MTs, there are specialists in humanities and there are just citizens who were requested by our Ministry of Health, Mme TOURRAINE to assess the situation in terms of vaccination in France with the reach and made over the last years. The confidence in vaccination has dropped a little bit and our task, once we have finished our work, is to make recommendations to the Ministry about how to improve the confidence in vaccination in France.

So, to do so, we are doing several things: the first one is exactly what we are doing today with you and other people, that is to have interviews with experts ; we are gathering documents, and we have an ongoing dialog about the present opinion of French people about vaccination ; and, above all, we have a comity of ordinary citizens as well as a comity of professional workers in health to make recommendations to us about the situation of vaccination in France. This is the context and, obviously, the key aspect is the hesitation of many people about vaccination, so we are extremely interested to hear you, given your vast experience in that topic, and to have a discussion with you about these questions.

Madame LARSON – Okay. I tried to make the slides not too long so we can focus on discussion. Basically, the timing is very good, because, and I will talk a little more about it, but tomorrow we will releasing an e-biomedicine in 67 countries on vaccine confidence. You are the headlines. I will talk more about it, but France, of the 67 countries, was, not by a small margin, the absolute least confident country in vaccine, particularly safety, but also its effectiveness.

I'll talk a little more about it later, but I think it can give you a global context a global context for your report.

Monsieur FISCHER, President. – Absolutely. Can I ask you tomorrow how we can access the report?

Madame LARSON – It's online, I'll send you all the links. We have a lot more behind it that we can share with you. I'll give the top of slides to give you a sense of what is driving the work of our group. Basically, when people have the supply, the access and the information, what is more difficult is to measure the emotional factor along the issues that you, as a country, are dealing with now. It's not a rich country issue either; we are seeing it also in the two states in India with the highest education and economic profile: those are the states with the strongest anti-vaccine groups. It's not only a uniquely rich-core country divide, in terms of the luxury of complacency or refusal. It's a very strong ideological and political issue.

I should say that while France was absolutely the least confident of the 67 countries, the region which was overall sceptical was Europe, and particularly, next to France, Bosnia-Herzegovina and Eastern Europe in general. 7 of the 10 least confident countries were in Europe, if you include Eastern Europe. The point I make in the paper, but also in the press release that I'll also send you is that we should not underestimate the impact of this in terms of global influence. Between social medias, Internet, all the rest, with global translate these days, the threat is global and not just around French speaking Africa, and even if Google Translate works better with French, now, any imperfect translator does not help with the accuracy of information traveling.

In the next slide, which is most of all the work of our project, I'll show you that when we look into the field where the work is going on, there is a lot of work on the individual dynamic between patient and provider. There was very little work on the transnational, the social network, the group influences and the global picture. So, we have been focusing on those dynamics, both social and group influences, and also everything that was focusing on measureless. Metrics bring together combinations on media and social media monitoring survey work, quality of research. We have 247 systematic review of any new literature coming out and we bring that all together to try and get the largest picture possible. We learnt: earlier in the game, ten years ago, it just started with media monitoring: now pieces of information can tell you the whole story, don't just rely on media monitoring, don't just rely on surveys. We really focused on monitoring things over time, because one thing about the nature of the

topic we were looking at is that it is highly volatile. The closest thing I can think of is political opinion polling. If you do a survey in January, don't expect it's gonna be the same in December or the following February. There will be some hard-liners who are persistently negative or positive, but you will get merging issues and unspoken opinion leaders that change the opinions. We are also looking at who these particularly unspoken leaders are.

The next slide points out that ten or fifteen years ago, I was heading UNICEF's global immunization communication and I saw the growing emergence. I ended up extinguishing different fires in different countries around issues with vaccine confidence. It was not just individuals, it was countries, it was groups, it was governments, and it was different groups. And I went to WHO to say that we had a problem, but I was not getting much reception. They said that we had just to be more positive. But, 5 years ago, so many countries went to them asking for help on this issue, I'm sure you've seen it in your review, which they set up an advisory group to the immunization group. We generated a lot of the reviews on what was going on. We have a problem.

By the way, there was an article published last month: a group from the University of Michigan showed that one of the things that we see is not a trust problem, but the fact that people feel they do not benefit from sufficient information. They only get part of the information, safety part of the information about the vaccines. Those researchers took two or three groups of people ; one got the standard one-page CDC overview on HPD vaccine, one got pieces of paper with some supplementary material, and the third one was given full detail on the number of the cases reported suspected adverse effects that people had filed online. The hypothesis of the researchers was that if people were given all the information, they would trust more. Indeed, they found out that there were more confidence in the second group. So information is good, but not too much information.

I was asked to write a perspective piece in Science magazine that will come out next week on why information is just not enough to address trust.

The other thing I mention in the next slide is that impulses don't happen the next day. Sometimes, an event happens and, after a few weeks, polls don't show big reactions. But months or even years later, as the information spreads, things happen. So, a while ago, there was a confusion in an article with a deeply scientific research article on a contraceptive vaccine that said in it that tecnis toxylite would be used as an approaching career: someone mistook it and explained that this contraceptive vaccine was a sterilizing vaccine. It was faxed to 60 countries in a pro-life catholic organization. It created panic around the world. it generated problems in South America. The WHO headquarters in Geneva had to go sit down with the Vatican asking them to speak because they would not listen to anyone but the Vatican. It was a lot of work, not unlike what we did about polio 10 years after that.

The point about this slide is to say that it took years for the overall coverage of tecnis vaccination to drop.

In the next slide, I look at the same phenomenon with the MMR vaccine that was under suspicion after an article published by Wayfield in 1998. And the actual lowest point of vaccine coverage after that was 5 years later ; and it was only last year that the coverage rate of MMR, fifteen years later, got back to the same level as before the article. Sometimes, you see an immediate panic after an attack before a slow comeback to the precedent rate, but sometimes these are slow-burn erosion of people's confidence. It takes times. As a ministry of Health, I think vigilance is the key. Don't ever underestimate what the longer-time impacts can be. Some of these perceptions are traveling around the world. Malaysia is a very strong anti-MMR group now, as if they discovered the Wayfield's story last week. It's important to follow this global story. As you may have heard, Wayfield has now become a filmmaker and he is showing is new film in the US. He has gained a lot of credibility to spread his ideas.

So this is unfortunately going on.

One of the things we've seen in our research is that sometimes the solution lies outside of the vaccination program. There is a combination of some events in the vaccination program, under the line of governments, producers or bad experiences. There are multiple levels to follow. Immunization is a very vertical program, even inside health, and we need to make more friends outside of just our circles, and particularly outside of vaccine and immunization circles. I often think about the AIDS response in the absence of either a diagnostic or a cure many years ago: the modelization of partners was really vital, and we need to think about who are the influential people, who are the ne networks that can bring confidence.

We have very changed publics, dramatically changed by ten years ago, even. There is a sense of very thin empowerment. People think they have voice because of social media and feel frustrated because it has no impact on our policies.

In the next slide, just as an example of this, it's not even outside of the immediate program, locally and nationally, but it sometimes involves global networks. That was the analysis of the polio boycott in Northern-Algeria. In the dossier of documents that they gave to the people from UNICEF to rationalize their polio vaccine boycott, the document on the top was about the fear of sterilization about this tecnis program I mentioned earlier. Ten years later, almost twenty, that story resurfaced in Northern-Algeria to rationalize a boycott policy about a totally different vaccine, in a different country.

A current issue is HPV. We're spending more and more time on it. I know it's also a big issue in France. If you look at where Europe is, this is about the influences beyond local that contributed to the suspension of the HPV vaccine by the Japanese ministry of Health. They didn't suspend the provision of the vaccine, but the recommendation only. They said: "We do not want the liability of recommending it,

but if someone demands it, we will give it to them at no cost, but we don’t want to be responsible for having recommended it”, which is an even more ambiguous and confusing picture.

It is now that well over three years, they have many times gotten close to bringing it back. The organization of gynecologists, obstetricians, pediatricians have all appealed to the ministry of health to bring that vaccine back, they got no media coverage. The media coverage is with a very strong and proactive anti-vaccine group that call itself victims of injuries or victims of HPV, and it’s the mother of what was originally 12 girls became a number of others who is highly networked in the Japanese parliament.

When I talk to people in the diet, they say that they all know about Denmark. Denmark is a highly, highly active influence on the Japanese suspension. Of course, as Japan has suspended it, it has become part of the appeal of several countries that are claiming for a suspension. I read an article in Nature about how different governments have responded to very similar reactions and I used it to analyze the situation in the UK and Colombia which have had about 500 girls reacting with kind of fainting. They both stood up to the science and where India and Japan benched to public pressure and suspended their HPV, programs are… I can send you this article.

This is a global picture, and this study is an important one in the light of the research we will publish tomorrow to not underestimate the impact of the low-confidence in France and Europe on other countries. Those countries look up, particularly with the amount of vaccines produces between GSK and Sanofi and other companies in Europe ; it’s a place where they look for better vaccines and we should not underestimate the potential in a longer-term influence.

I’m sure you are familiar with what Denmark has done in Europe, which is to push the European Health Agency to do a re-review of the safety of the HPV vaccine. That study was published last November and it was on that occasion that Nature asked me to write this piece I mentioned. Since then, the Nordic group has written a critic not really accepting that report and EMA has responded to it. There are still considerable tensions and a lot of emotions around this issue, because the girls and the parents are under a real amount of stress that we cannot acknowledge. It was a real situation for the girls. The question about the connexion with the HPV vaccine has been studies in several countries, including in Japan, and the conclusions show exactly the same rates of these symptoms among the girls that were vaccinated and the ones who were not. I think the suspected links with vaccines are actually helping the public health community to discover bigger underlying issues. We need to pay attention to what is going on with these events and, only when we are able to answer better to those issues will we be able to alleviate some of the anxieties to the vaccines.

The next slide shows some of the reactions to the report that was not easily accepted, particularly by some people who refuse to change their mind. One of the

things in last year's state of vaccine confidence report is that confidence in the Health system is very important for confidence in immunization. If you don't have confidence in the system, we find it directly correlated to level of less confidence in immunization. What do we do about it is stepping back from the vaccine program and looking at how the system is delivering and responding to the citizens. In the case of HPV vaccine, in France, I mean, you have have the three Hies, that go across childhood, adolescence and adulthood, and the interactions with the health system are very different, particularly for adolescents that are just on the edge of pediatric treatment. Pediatrics are sometimes uncomfortable about this vaccine. There is not a routine checking for adolescents, really, besides for what gets to sexual and reproductive health, which concerns an older audience. So, how is the system responding? That is a question I would ask.

The flu vaccine is another issue, but it has the worst unhearance around the world.

We've done quite a lot of work in the last years with ECDC that have recognized that there were significant issues, in Europe. They want to basically to have a more Europe focused vaccine hesitancy review. We have done further researches in four countries, including France. As you can see, one of the areas where there is very low trust is in the information provided. Now, I think one thing as an action would be to understand why. Informations are pretty broad-categorian. I wouldn't look at that saying "We need more information". I think that we need to understand what, in the information, is missing. Is it the content? Is it a matter of who is delivering the information? The amount of information in group experiences shows that too much information can be unproductive. Sometimes, people feel that you are not listening to them when you try to show more information.

You will see the complete technologic report en ECDC website. Vaccine safety is overwhelmingly the biggest concern.

You may have seen this slide and I won't spend too many times on it, but it is what we developed at the global review of issues. When there is an issue to understand first, it is specifically about the vaccine, and is it about some group ou individual influence or is it something that is more contextual, linked to political or religious issues? Some of them are beyond the scope of the immunization program, but you have to medicate the negative influences. Where the drivers are coming from is important to understand what you can do about it.

We developed what we call a diagnostic tool. We came up with a list of what we see, typical things that can prompt rumors and misinformation. One is adverse events. Whenever there is a suspected adverse event, it will heighten questioning and anxiety. When there is a piece of new research, there are always new questions. Be ready for questions around that. Any new recommendations or policy change will raise questions. You just need to be ready when answers are not scientifically supported, but that there is some level of acceptability and consideration when they are introduced. Sometimes, having a smaller focus group around a new

recommendation allows anticipating some of the questions is a good approach. One thing the European Medicine Agency found very helpful was a media-monitoring. Over a four months period, we gave them the topics that went up in the media across Europe about HPD, and they said it helped them a lot to anticipate the kind of questions that they would be getting when they released the HPD safety review.

Whenever a new product comes out, it always raises questions. You have to be ready for them. People want to know the accuracy of new products and research.

And then, you have to pay attention to political motivations. Sometimes, people make connexions that governments should do is to pay attention to negative things that pop up, articles, individuals, media, vaccine refusals. Because, sometimes, an expression of this kind can have a no-effect and the next-one do a lot of damage. It is important to pay attention to the geographic spread. When rumors or anxiety start somewhere, you start to see the popping-up in a few different places. What we see more and more is a anti-vaccine sentiment linked to anti-GMO groups that are taking that as a new cause. Those groups are particularly concerning, because they already have highly developed networks.

One of the areas that I mentioned is that we do a 24-7 global media monitoring, keeping the pulse on what the current issues are around the world, on the tone, etc. We were only focusing on online business media, because we didn't think at the time that social media was global enough, but we are more and more including social media, as they spread around the world.

The next thing is that we separated the positive reports that are in blue and the negative reports, which are red. We disaggregated further by vaccine. In France, it is reasonably balanced, but it was quite negative, as it was at a time when you had a lot of cases. Today, the dial would be different in terms of which vaccines are more positively or negatively considered.

As I mentioned, the other thing we do is monitoring issues over time. To show you an example, I was asked to go to beijing last week to meet with their Ministry of Health because as you saw on the news, they have an absolute major vaccine scandal with a pharmacist, over the last ten years, setting up maybe 2 billion dollars reselling and expired vaccine. We were working on how to build back the confidence. I mention it as an example of looking at how those issues evolve in time.

We have done similar things around clinical trials. In Ghana, there were a number of rumors which basically shut down the face one trial, largely politically driven, but it shows you the way things went. We are about to publish this study with broader explanations. It is really important to know where the sentiment is mostly being felt from.

In the last slides, I just wanted to give you a glimpse on what is going to be published tomorrow. Basically, there were four statements and four options going from strongly

agree to strongly disagree. We had a total representative sample about 66.000 people around 64 countries. Overall, people's confidence about the importance for children was reasonably high, including in France, although is was lower than in other countries.

The next question was about safety. There is a lot of reluctance about this issue. The global average percentage disagreeing with the idea of vaccine being safe was 12% but the rate reached 41% in France. It is three times the average rate. It is dramatic. I was expecting skepticism, but not that much. I was quite surprised but the extent.

About the effectiveness of vaccines, the answer was a little better than for safety. In France, 17% disagreed on the fact that vaccines were effective. This is still half of the 41%. 12% disagreed on the fact that they were important.

The last statement we included was: vaccines are compatible with my religious beliefs. That was just 11% in France, but it is an area we need to look further into, because we found out that the same religion, at an individual level, can lead to different answers depending on the location where you live. You can be a Muslim in different country and have a different opinion on this matter. It's not surprising.

You really need different sources of data, surveys, medias, to get the full picture. Tomorrow, we will give you the links to the new articles. That's it.

Monsieur FISCHER, President. - Thank you very much, this was really a performance. A lot of information, not good for us, but, at least, it is a further reinforcement that the work of our group is more than needed. There is a lot to do everywhere in the world, but, unfortunately mostly in France. I have a curiosity question about the distribution of the opinion about safety in France. How is the overall distribution? Can you detect heterogeneous groups? Do you have enough people to make such statistics?

Madame LARSON – Well, for France, we had 964 people. Overall, the samples were the same in all the countries. We do have all the individual data, so that we can look at it to give you any answers. Someone else asked me a question about whether there were gender differences. Surprisingly, there wasn't many differences in gender responses on these questions, unless there were more women that strongly agreed about the importance of vaccines for children. We can look back at the global average. We can come back to you with more details.

Monsieur FISCHER, President. - If you don't mind, we might come back to you with specific questions about the situation in France, if it is possible, given the fact that you have been able to collect quite an amount of information. You mentioned that, in order to improve confidence, it's needed to get more friends outside of the Health circles and you took the example of AIDS. I find it very interesting. For me, for AIDS, the good friendly people were the patients themselves; in the case of vaccination, I

don't spot the population that could be friendly, because there are no patient, there. How do you translate that for vaccination ?

Madame LARSON – There was a very strong patient movement for AIDS. I was thinking that the most extreme case was South-Africa, because the President was in absolute denial, and they mobilized everyone. If you are trying to mobilize better support for influence of vaccine and older adults, to look at what where things are circulating, you can try to take advantage of those networks. Schools are one thing, but one of the places where you can reach young people and make this kind of position is on the social media. You need to look where the people are the more hesitant. Are those people going to church? This is unlikely, these days, but you can try to find out the professional groups involved and act on that by identifying different kind of circles.

Anne-Marie MOULIN - You mentioned rumors about vaccines in Africa, Asia and America: those are countries very far from each other and very different. Can you make the difference between rumors caused by active propagation and similarities of structures?

Madame LARSON –Most of the time, it is accidental, like in the case of total misreading of an article. In the case of Japan, it was propagated by the mothers of the girls who had had a real experience. Something triggers it, and then there is a feel that keeps it going. The nature of rumors can be different, but there are similarities. The thing is that the news in the world are getting homogenous. It's like we get more and more international brands going on, with a bit of homogenization of these concerns.

Monsieur FISCHER, Président.. Can you analyze which effects have been involved positively to restore a satisfactory level of confidence? Have specific measures been taken ?

Madame LARSON – One of the thing that helped was that the Ministry of Health started doing pulse surveys, initially four times a year, to try and understand what the public was feeling about this vaccine. It is similar to the flu surveillance that has been implemented in France by Patrick Kanner.. England learnt that you cannot wait so long to react to those things, because uncertainty is the worst thing that can happen. In the case of the HPD case, England reacted way quicker.

Monsieur FISCHER, Président. – But who should be the prompt reactor, if I may say so ? In France, if there would be a prompt reaction by the ministry, the level of trust would not be that high. Maybe it would be different in the UK. What do you think ? Do you think that today, the Public Health Agency, autonomous from the government, could earn the trust of the public?

Madame LARSON – It is a very good point. We have a similar structure in England that relies on the government. You do need some official reactions. It is a bit of a

problem when you get silence from official sources, because people get even more suspicious.

Patrick ZYLBERMAN – It was somewhat different in England, because Wayfield was sued and condemned severely by a Justice court. He was forbidden to teach, to publish and to make any scientific research public. Such things never happen in France. Pr Joyeux was likely condemned. It was highly a reflexion of the Conseil de l'Ordre, but there was no action before a Court.

Madame LARSON – Unfortunately, he started another life in the United-States. Sometimes, when people are treated too severely, they become martyrs for the anti-vaccine. Many scientists, after publishing something like that, can acknowledge that they were wrong. Wayfield, to this day, insists on saying his work was correct. The more he gets kicked out of the University, the bigger is audience, as he started filmmaking, now.

Someone from the audience – Thank you for your presentation, and we are struck with the figures of France. The impression we have in France is that the negative perception above vaccine is not a general perception about vaccines, but concerns some vaccines. The vaccine coverage grows for some vaccines at the same time as it is diminishing for others. Is this focused mistrust something shared all over the world?

Madame LARSON – Yes, you are absolutely right. It tends to be issues around specific vaccines, except when the groups focus on the vaccines themselves. In general, you are right. One of the things that struck me, particularly in France, is that people agree on the fact that vaccines are important for children but think that vaccines are note that safe. This might be part of the discrepancy. It could have been nice to ask about each vaccine and try to know if, in the end, people took or not the vaccine, but we didn't do it for this report. It would be interesting to dive further in the national countries reality.

Madame LARSON – I think it was an important thing, and we need subnational surveys in the US, but if we take surveys at a state level, we will have big differences. Actually, the vaccine scare in California had a bigger profile because of Disneyland, but it was not that big. There is a big issue in pockets from the different states, but a study at a state level would be too gross to be relevant.

Monsieur FISCHER, Président. – Thank you very much.