Cullenagh
Portlaoise
Co. Laois
20th January 2011

Dear Ms. McCann,

Thank you for forwarding a copy of Tony Holohan's letter regarding Gardasil vaccination and thank you for taking the time to consider my argument on this important subject.

I would like to lay out my reply to Dr. Holohan quite simply in this letter and I would also like to backup my statements with relevant references and additional information below. I have included my own comments on these references typed in blue.

1. Vaccines are given , in general , to healthy people. It is doubly important, therefore, that they are safe and effective.
2. Vaccines are always associated with some risk of adverse reaction, as are all drugs.
3. This risk must be weighed up against the benefit.
4. Gardasil is a new vaccine and the risks and benefits are not fully understood yet.
5. The efficacy of Gardasil is modest and has been exaggerated.The vaccine has not been adequately tested on the age group to which it is given.
6. Many safety concerns have been emerging particularly in relation to auto-immune diseases and over 80 deaths have been reported in association with the vaccine to the USA VAERS system.
7. The National Immunisation Office has publically stated that the vaccine has been associated with *no deaths or serious adverse reactions.*
8. Parents are therefore being led to believe that the vaccine presents only benefit to their child.
9. This is misleading and does not allow the parent make an informed choice for their child.

I would strongly urge this committee to ensure that the correct information regarding this vaccine is disseminated .

As Joint Oireachtas Committee on Health you are the people's representatives and are obligated to act in a way that ensures the safety of the people and that our human rights are upheld. These rights include the right to make informed decisions regarding our health. The NIO has acted, in my view, as an advertising agent for Merck with it's unchallenged promotion of this vaccine and it's lack of critical thinking on the matter. It is up to you as legislators to balance this out. If, in the future, we have cases (and statistically this is a matter of when rather than if) of vaccine damage from Gardasil then the HSE and NIO may be leaving themselves open to legal action. Any young girl damaged by this vaccine may have a very strong case having been told that this unique vaccine was free from any risk.

Yours faithfully
Paula Byrne

1. Vaccines are usually given to healthy people, therefore it is doubly important that they are safe and effective.

“ Vaccines are different from most other medicinal products in ways that influence safety considerations. pre- and post-exposure vaccines against infectious diseases are a preventative measure, usually given to healthy individuals and especially to young children at a vulnerable age. They have a complex composition and a short duration of exposure with a long term response. No (immediate) health benefit might be apparent to the individual vaccinee due to the success in reducing illness in the community. As a result there is limited acceptance of any potential risks” **Guidelines on the conduct of pharmacovigilance for vaccines for pre- and post exposure prophylaxis against infectious diseases. CHMP EMA (European Medicines Agency)**

2. Vaccines are always associated with some risk.

“ No vaccine is however 100% safe”**Guidelines on the conduct of pharmacovigilance for vaccines for pre- and post exposure prophylaxis against infectious diseases. CHMP EMA (European Medicines Agency)**

“ Since the inception of vaccination it has been recognized that Adverse Events following Immunization (AEFIs) will occur” **WHO Global advisory Committee on Vaccine Safety; Causality Assessment of AEFIs**

“No medicinal product is risk free” **IMB website**

“ No vaccine is without side effects” **Drug Safety Newsletter May 2010 IMB**

3. The risk must be weighed against the benefit.

4. Gardasil is a new vaccine and the risks and benefits are not fully understood yet.

“ Serious and clinically relevant adverse reactions are mostly rare and thus are unlikely detected prior to marketing as the sample size of clinical trial database is mostly limited to detect common and uncommon adverse events.Long term follow-up of vaccinees might also be limited and pre-authorisation data will most likely address concerns of long term risks. Furthermore, in pre-authorisation clinical trials the study population is highly selected, whereas, in the post-authorisation phase immunisation might be targeted at a heterogenous population with diverse backgrounds diseases.**Guidelines on the conduct of pharmacovigilance for vaccines for pre- and post exposure prophylaxis against infectious diseases. CHMP EMA (European Medicines Agency)**

“As rare but serious adverse reactions, reactions with delayed onset and reactions in subpopulations are usually not detected prior to marketing authorisation post-authorisation evaluation of safety in studies is critical for vaccines.”**Guidelines on the conduct of pharmacovigilance for vaccines for pre- and post exposure prophylaxis against infectious diseases. CHMP EMA (European Medicines Agency)**

“ The duration of protection is currently unknown” **Gardasil Package leaflet for the user.**

5. The efficacy of Gardasil is modest and has been exaggerated.The vaccine has not been adequately tested on the age group to which it is given.

“Impact of Gardasil on the incidence of CIN irrespective of HPV type-
CIN1 or worse- 13.7%
CIN2 or worse-12.2%
CIN3 or worse-11.2%
There appears to be little benefit in the MITT3 population....The MITT3 population may be considered to approximate the general population of women who are naive and non-naive , some of whom may have HPV at baseline’ **Clinical review of biologics license application for human papillomavirus 6,11,16,18 virus-like particle, manufactured by Merck.. Centre for biologics evaluation and research, Food and Drug Administration.**

This is an important, if complex, point to understand.The subjects in the trials of Gardasil were obviously divided into those who received the vaccine and those who received a placebo. They were further divided into several groups depending on whether they had been found to be negative to previous HPV exposure or positive. In other words if they were already infected with HPV or not. As HPV is a very common infection, about 80% of adults will have been exposed to it throughout their lives.

You will probably have read of efficacies for Gardasil of up to 100%. These percentages were in groups which had been screened and found to be negative to HPV before being vaccinated.

It is also important to understand that percentages can be very misleading. For example in one section of the trials with almost 8,000 women in both Gardasil and placebo groups, one breakthrough case of HPV lesion in the placebo group is considered to be 100% success for the Gardasil group!

Because the vaccine was so *unsuccessful* in preventing lesions in a group which approximated the average population it was decided to give the vaccine to younger children who would be less likely to have been exposed to HPV through sexual activity.

However the vaccine was tested on very few under 15s and there were only 355 12 and 13 year old girls enrolled (the age group to which we give the vaccine in Ireland). These girls were not tested for efficacy, that is, did the vaccine prevent cervical lesions, but were merely checked for seroconversion. Seroconversion means that they developed antibodies in their blood indicating exposure to the HPV vaccine.We know from other vaccines, notably tetanus and whooping cough, that high levels of antibodies do not equate, necessarily, with protection from disease. As Gardasil is a new vaccine it’s efficacy in this age group is therefore based solely on assumption.

In Ireland our policy has been based largely on the recommendations of the **HIQA report** on Gardasil. Some politicians have stated that this report estimates that Gardasil vaccination will result in the reduction of deaths from cervical cancer by 52 per year. This seems pretty impressive but this is not what the HIQA report claims. *52 deaths per year may be averted by a combination of screening (Pap smears)and vaccination.* However it is regular and routine screening which will cause the reduction in deaths with only a tiny (and theoretical) contribution from the vaccine. Screening has not been offered routinely in this country till 2008 and therefore will reduce the current death rate from cervical cancer in Ireland by up to 80%.

6. Many safety concerns have been emerging particularly in relation to auto-immune diseases and over 80 deaths have been reported in association with the vaccine to the USA VAERS system.

At the 13th annual meeting of the American Neurological Association researchers describe a case of rapidly progressive disease leading to the death of a 14 year old girl." *Pathological features support the temporal association of the clinical presentation and vaccination and provides supporting evidence that immune-mediated reactions to the nervous system are potential risks after Gardasil vaccination*." **Catherine Lomen-Hoerth MD, director of the Amyotrophic Lateral Sclerosis at the University of California-San Francisco** told the meeting. " Our patient received three doses of Gardasil with symptom onset 2 months after her last dose. Despite treatment with aggressive immuno-suppression, her weakness relentlessly progressed and she died of respiratory failure 21 months after the onset of her weakness."

In September, investigators presenting at the **European Committee for Treatment and Research in Multiple Sclerosis** annual meeting reported cases of autoimmune disorders after immunization with Gardasil.

Presenter **Maria Bouktsi from the Interbalkan European Medical Centre in Thessaloniki, Greece** told **Medscape Neurology** that her team is questioning whether the immuno-stimulatory of the HPV- like particles of the vaccine are triggering adverse effects in vulnerable patients.

It is the same question that researchers asked in a recent issue of **Multiple sclerosis (2009;15 116-119). Ian Sutton from St. Vincents Hospital, New South Wales, Australia**, and his team have reported five cases of multiple sclerosis after vaccination with the drug. The team reported that patients presented with *multifocal or atypical demyelinating syndromes within 21 days of immunization.*

It is important to not that these researchers have noted an unusual or unusually rapid development of disease that is not normally seen in the general population.

In a recent letter to the editor of the **European Journal of Neurology S. Blithshteyn of the Dept of Neurology, State University of New School of Medicine and Biomedical Sciences, Buffalo , NY, USA** described a case of Postural Tachycardia syndrome (POTS) following vaccination with Gardasil. POTS is thought to be an auto-immune disease. The symptoms include dizziness, exercise intolerence, fatigue, nausea and loss of appetite which in this case has lasted months. The patient had no other relevant factors or events preceeding the symptoms onset apart from Gardasil vaccination.

This is a significant piece of research as symptoms of fainting and dizziness are the most common adverse event to Gardasil and have been, somewhat dismissively and misogynistically, been reported as "psychogenic". Dr. Blithshteyn says " it is probable that some patient who develop POTS after immunization with Gardasil or other vaccines are simply undiagnosed or misdiagnosed, which leads to under-reporting and a paucity of data..."

7. The National Immunisation Office has publically stated that the vaccine has been associated with *no deaths or serious adverse reactions.*
8. Parents are therefore being led to believe that the vaccine presents only benefit to their child.
9. This is misleading and does not allow the parent make an informed choice for their child.

Additional Information

1. Other Countries

I would like to present some additional information from other country's experience with Gardasil.

France
On August 31st 2010 Merck's marketing partner for Gardasil, Sanofi-Pasteur, was officially prohibited from advertising Gardasil for cervical cancer prevention in France. The Director General of the French Agency for Safety of Health Products (AFSSAPS) found the sponsor of several Gardasil ads to be in direct violation of French public health codes. These violations included, but were not limited to:

- Claiming longer efficacy that was actually proven. "The ads stated an 8.5 year efficacy period when, in fact, the only data of validated efficacy is limited to a maximum assessment of the effectiveness of 4.5 years"
- Making false claims: The ads in question replaced the officially approved use of Gardasil for "the prevention of low-grade lesions" with statements indicating Gardasil be used for " the prevention of pre-malignant genital lesions, cancers of the cervix and external genital warts"
- According to the French Committee on Immunization Practices (CTV) and the High Council of Public Health (HCSP) " the vaccines impact on the incidence and mortality of cervical cancer will only become apparent in the long term, in fifteen to twenty years..."

Although Ireland does not allow the direct advertising of Gardasil in this way the National Immunisation Office has essentially been advertising the vaccine by highlighting exaggerated benefits and by it's uncritical acceptance of the claims of the drug manufacturers. The NIO should be a formidable champion of the people's health and not the lackey of the pharmaceutical industry.

Spain
In February 2010 Spain's Health Minister ordered hospitals and chemists to temporarily halt the use of a batch of Gardasil after two girls became ill after a shot.

India
In April 2010 the government of India called a halt to trials of HPV vaccine in the country.This followed reports of ethical violations within the trials and public outcry at deaths and side effects reported from use of the vaccine by a fact finding visit to the areas concerned.

2. Limitations of Drug Monitoring Systems

It is important to understand the limitations of the systems of drug monitoring upon which Tony Holohan places so much faith.

- "Causality assessment is complex...in most cases there are no specific tests to prove a causal association between a vaccine and an Adverse Event Following Immunization (AEFI).In contrast there may be several tests that can confirm an event is due to a specific cause other than Immunization, ie., a coincidental event" **CIOMS/ WHO Vaccine pharmacovigilance working group**

- “The clearest and most reliable way to determine whether an adverse event is causally related to vaccination is by comparing rates of the event in a vaccinated and a non-vaccinated group in a randomized clinical trial. Such trials ,however, can never be large enough to assess very rare events, and post marketing surveillance systems are required to identify events potentially related to vaccination” **Global Advisory Committee of Adverse events following immunization, WHO**

- **“**Clinical review of GBS (Guillaine Barre Syndrome) included 52 cases reported to VAERS... In Summary the limitations of these studies included the usual limitations of VAERS... so post immunization rates of TM (transverse myelitis) or GBS cannot be calculated” **CDC Advisory Committee on Immunization Practices, Summary Report October 22-23 2008 Atlanta, Georgia, USA**

-“Comparisons with expected rates of GBS, however, were inconclusive for an increased risk, and lack of controlled epidemiological studies make it difficult to draw conclusions about a causal association” **Vaccines and GBS; Haber et al, Drug Safety 2009;32(4) : 309-23**

- “ Appropriate case definitions and validated analytical tests for confirmation of the infective agents should be used wherever possible. Case definitions for vaccine failure, lack of effect, break-through infections are not universally agreed at present, but it is expected that consistent case definitions will be published in the near future by the CIOMS/ WHO Wroking Group on Vaccine Pharmacovigilance.” **Guidelines on the conduct of pharmacovigilance for vaccines for pre- and post exposure prophylaxis against infectious diseases. CHMP EMA (European Medicines Agency)**

3. **Withdrawn Drugs**

I would like to point out some of the drugs which have in the past, gone through clinical trials, been approved by the Competent Authorities and later withdrawn due to safety and/ or efficacy concerns. These include:

-Thalidomide withdrawn in1960s
-DES withdrawn in 1970s
-Vioxx withdrawn in 2004
-Acomplia withdrawn in 2008

This obviously indicates that it is not unusual for a drug to have reached the current status of Gardasil when in fact their risks outweigh the benefits.
In the UK Gardasil is classified as a “Black Triangle” product . This classification is given to newly licensed drugs in the UK which are monitored closely in order to:
- confirm risk/benefit profiles
- increase understanding of safety profiles
- ensure previously unrecognized side effects are identified as quickly as possible.

In other words, despite Tony Holohan’s assurances to the contrary, as far as Gardasil is concerned, the jury is still out.

4. Adverse Reactions Reported in Ireland

Finally the IMB has had many adverse reactions reported to it since commencing vaccination. These have included serious AEFIs such as convulsions, paresis (partial paralysis), alopecia (hair loss), anaphylaxis and significantly one case of GBS. This case was reported in the IMB line listing of October 2010 but was changed by the November listing , which did not include the description of GBS for the patient. I have asked for clarification on this matter and been advised by the IMB the "The patient was discharged from hospital following investigation which revealed no abnormalities and has now recovered....without a diagnosis of GBS established or confirmed". Not having GBS established or confirmed is quite different to having established that this was not a case of GBS. GBS by its nature can be transitory. I have further asked the IMB if this case has been reported to the EMA as a case of GBS or not but to date have not received a reply. The **EMA Guidelines for Marketing Authorisation Holders, Competent Authorities and the Agency on the Electronic Exchange of Pharmacovigilance Information in the EU** states that "On receipt of further information that the case was not medically confirmed....The case should not be nullified"

To conclude, I hope all of the above will convince the Joint Oireachtas Committee on Health that claims that the Gardasil vaccine has been asssociated with "no deaths or serious adverse reactions" is untrue and that you will seek that the NIO make the plain truth of the matter available for parents so that they can make a properly informed choice.