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To Whom It May Concern:

I am writing this letter in support of Dr. Jovana Stojkovic, who is under threat of losing her medical license due to questioning the exact safety level of the immunization programs.

Let me first present our background. Our clinical and research group (Henri Mondor Paris Est-Est University Hospital, INSERM U955E10) has been working on vaccine safety issues for more than 20 years. We have conducted both clinical and experimental research on the topic of Aluminum adjuvants..

Clinical research.

-We have first described a specific muscle lesion called macrophagic myofasciitis (MMF) (Gherardi 1998).

-Then we provided evidence that this lesion assesses unexpectedly longstanding persistency of vaccine-derived aluminium hydroxide particles within immune cells called macrophages, detected at site of previous immunization in a small proportion of vaccinnees (Gherardi 2001).

-Adult patients with longstanding MMF were shown to suffer from chronic fatigue, diffuse myalgias and cognitive dysfunction meeting international criteria of myalgic encephalomyelistis/chronic fatigue syndrome (ME/CFS) (Authier 2003). This syndrome likely reflects chronic low grade immunostimulation with eventual immunolgical burn out (Hornig 2015). MMF syndrome has been named "autoimmune/inflammatory syndrome induced by adjuvants" (ASIA) by Yehuda Shoenfeld in 2011(Shoenfeld & Agmon-Levin 2011).

-Cognitive alerations of MMF patients were found to be stereotyped and neither attributable to chronic pain nor to depression (Couette, JIB 2009; Passeri,JIB 2011; Aoun Sebaiti, JIB 2018).

-Consistent functional neuroimaging alterations were found, including (i) focal brain perfusion defects assessed by SPECT (single-photon emission computerized tomography), well correlated to both attention/memory alterations and inter-hemispheric dysconnexion (Van Der Gucht 2015); and (ii) a characteristic pattern of posterior cerebral hypometabolism assessed by FDG-PET (fluorodeoxyglucose -positron emission tomography) scanner, involving occipital cortex, hippocampus and cerebellum, predictive of MMF detection a muscle biopsy (Van Der Gucht 2016, 2017a,b; Blanc-Durand 2017a,b)

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In summary, We identified described an histological biomarker assessing that a given individual has difficulties to clear out the alumunium adjuvant from his immune system (WHO 1999). Clinical analysis has yielded highly consistent findings in these individuals, indicating that longstanding MMF is prominently detected in an homogeneous subset of patients with a stereotyped neuroimmune condition.

Basic research.

-We examined in detail the few articles on adjuvant toxicokinetics in the literature that serve as a reference for health regulators and industrialists to support contention that aluminum adjuvants cannot be unsafe. We found they strikingly suffer major conceptual and methodological limitations (Masson 2018).

-We showed in the lab that, in contrast to previous belief (Flarend 1997), Aluminum hydroxide particles injected in muscle are not solubilized in the interstitial fluid and vaccine derived aluminum is not quickly eliminated in urine: instead, this nearly insoluble particulate compounds are quickly captured by monocyte/macrophage lineage cells and can persist within these cells from many months after injection in animals (Authier 2006) to up to >17 years in some human beings.

-We also showed that, in contrast to the classical depot formation hypothesis (in which local deposition of the adjuvants was thought to play a crucial role (Marrack, 2009), a substantial part of the injected adjuvant is transported within cells to distant organs (Khan 2013; Eidi 2015) where they may persist as long as in the injected muscle (Crépeaux 2015). These organs include the regional lymph nodes, spleen and liver, and particles can eventually enter in the brain using a CCL2-dependent Trojan horse mechanism (Khan 2013; Eidi, 2015; Crépeaux 2015).

-We finally showed that, in contrast to previous belief that innocuity of aluminum adjuvants can be inferred from the low quantitities of Al3+ injected with vaccines (“the dose makes the poison” paradigm), neurotoxic effects of Aluminium hydroxide particles (Alhydrogel®) respond to a non-linear dose response curve with selective toxicity of the lowest doses (Crepeaux 2017). It seems that toxicity of this nearly insoluble particulate adjuvant which concentrates in immune cells may obey the specific rules of small particle toxicology rather than any simplistic dose-response relationship.

I strongly recommand you to reconsider the case of Dr. Jovana Stojkovic and her right to express her doubts because science is by no means sufficient and clear in the field of vaccine safety:

-WHO has long stressed that "*adjuvant safety is an important and neglected field. Since adjuvants have their own pharmacological properties, which might affect both the immunogenicity and the safety of vaccines, safety assessment is essential*" (WHO 2004).

-To date, however, aluminum and other adjuvants have still not been the subject of any official experimental investigation, and this being in spite of the well-established neurotoxicity of aluminum. There has been only one experimental study on aluminum adjuvants toxicokinetics (Flarend, 1997) and, as stated above, this unique study, as well as the two theoretical studies also used as "reference" studies (Keith 2002; Mitkus 2011),suffers major conceptual and methodological limitations [Masson 2018]. It seems highly mandatory to conduct new experimental toxico-kinetics studies, including long-term studies in a significant number of animals, under the tight control of health authorities, in order to ensure a maximum level of safety of both classical and new generation aluminum adjuvants used in vaccines.

-In the same way, aluminum adjuvants safety has never been epidemiologically evaluated on the long term. The US Centers for Disease Control and Prevention have recently stated "*there have been no population-based studies specifically designed to evaluate associations between clinically meaningful outcomes and non-antigen vaccine ingredients, other than thimerosal*" (Glanz 2015). (Thimerosal is and organomercury compound used as anti-septic preservative of vaccines). Intriguingly, the authors have demonstrated the feasibility of epidemiological studies aimed at evaluating the potential role of aluminium adjuvants in autism, but did not carried them out (Glanz 2015).

-The history of vaccines was largely built on an empirical basis during the last century. This was specifically the case for the aluminum-based adjuvants introduced in 1926. These adjuvants have been administered to the general population with continuously increasing rate since 1985 (along with successive introduction of adjuvanted DTP, HiB, HBV, HAV, pneumoccocus, meningoccocus and HPV vaccines) (College of physicians of Philadelphia, 2013). This was done without clear knowledge of their fate once injected in the body and no effort was made to clarify the point (Masson, 2018). Aluminium adjuvants are still intended to be administered to billions of individuals over the next years, because of massive expansion of vaccine prevention strategies announced worldwide, with> 270 new vaccines currently being developed and an annual

growth of 20% of vaccine business being expected by WHO (Kaddar 2012). The available studies clearly constitute insufficient bases to guarantee safety of aluminum adjuvants administered at such very large scale (Masson, 2018).

-The Institute of Medicine (IOM) indicated "*the evidence was inadequate to accept or reject a causal relationship*" for the vast majority of vaccine adverse effects they examined, and considered the limited number of good quality epidemiological studies and "*the inadequate understanding of biologic mechanisms underlying vaccine adverse effects*" as the major causes of uncertainty. The IOM committee declared that "*the value of dialogue between both epidemiologic and mechanisms approaches cannot be overstated. These conversations between different types of research can be difficult, but the results are worth it*"(IOM 2012).

The case of Autism spectrum disorders (ASD) : ASD is a neuro-developmental disorder of unknown aetiology. It is suggested to involve both genetic susceptibility and environmental factors that elicit strong or protracted immune cell activation during given windows of the neurodevelopment (Moris 2017). Children receive many vaccine doses in their first years over a reduced period of time, including MMR and Al-containing vaccines. Despite reassurances from health authorities and in the absence of official epidemiological studies dedicated to Al adjuvant safety at this age (Glanz 2015), the question continues to be raised about a possible link of Al-containing vaccines with ASD. Tomljenovic and Shaw (2011) found that the increase in exposure to Al adjuvants was significantly correlated with the increase in ASD prevalence in the USA, and that the amount of Al administered at 3–4 months of age was correlated with the prevalence of ASD in seven Western countries. Association does not mean causation but recent detection of very high levels of Al in the brain of autistic patients, which in addition was imaged and found intracellularly in microglia-like cells and other inflammatory cells (as in our mouse experiments Khan 2013), and not extracellurly as usual, leave the question largely open to discussion (Mold 2017). In support for a possible link, Al hydroxide-containing HBV vaccine administered at birth, a common practice in USA, has been shown to increase the risk of ASD by 3 fold compared to no vaccine or to delayed administration after one month (Gallagher et al., 2010). Such a stringent time window of noxious exposure fits well with theoretical ASD models. Moreover, in mice neonatal HBV vaccination results in transient neurobehavioral and neurogenesis impairments in early adulthood by inducing a proinflammatory and low neurotrophic

milieu in the hippocampus (Yang et al., 2016), and large animal studies have confirmed adjuvant safety concerns. In sheep, multiple injections Al hydroxide-containing vaccines or Al adjuvant alone can induce fetal losses, neuroinflammation and neuro-behavioural changes, including hyperactive states, aggressiveness, stereotypies, dissociation from the group and lethargy, which symptoms are disturbingly similar to those of ASD, along with winter increase of poor wellness markers, i.e. cortisolemia and WBC (Asin et al., 2018)

To conclude, I personally believe in the usefulness of vaccine-based prevention and I am even ready to accept the French mandatory vaccine program on the express condition that the strongly and urgently needed epidemiological and basic research investigations on vaccine safety are funded by and conducted under the aegis of democratically electected governments (Gherardi 2018). Unfortunately this has not been the case until now. In this sad situation, I strongly believe that you should consider as a fundamental human and medical right the possibility for any medical doctor like Jovana Stojkovic to publicly express reservations on mandatory vaccination.

Yours very sincerely

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Selection of significant publications from our group in the field
(other references available upon request)

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