

ATOINFO



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Gilles Chantrel & Jean-Philippe Massardier

«Accompany Life».

Whether at home or in hospital, to each and every patient, this is the goal of DTF medical.

This time, to accompany Special Forces on the field of complex operations where time mastering, device efficiency, easiness to use would trigger key chances of surviving, our Aerosotherapy R&D team once more got involved in an innovative yet ambitious challenge.

Discover AéroRiMac !



DTF. A Rhone Alpes based corporate invented the "anti-ricine" weapon !

DTF medical Aerosol therapy R&D unit based in Tours has been working on this project for 2 years, investing along with French Army Agency, roughly 250 000 €. Name code : Aerorimac. It is a nebulizing device allowing to inhale Ricine poison's antidote. This biological weapon kills very quickly by inhalation. The FAA had the antidote but one needed to find the way to nebulize it without altering it. "Our device had to impulse the antidote in the deepest part of the lung" explained Gilles Chantrel, co-CEO of the Rhone Alpes based company Diffusion Technique Française - DTF medical. Already disclosed at the FAA Innovation forum last November, the device will be produced and tested in 2013 on 1000 cases. "Possibilities could be greater than anti-ricine as biological threats are amongst main concerns of our countries nowadays" mentioned Jean-Philippe Massardier, Gilles' business partner. Other alternative options for this device could eventually lead to deliver antibiotics to children.

Stéphanie Gallo

► Press Release DTF-AERODrug & CEPRDecember 2012
Extracted from «Journal des Entreprises» -January 2013- translated into English.

«Inhale, you are saved»

A prototype of antibody nebulizer was selected to be part of the 10 prototypes presented on November 27, 2012 at the first Innovation Forum organized by the General Delegation for Armaments (DGA-French) at the CNIT (Paris) in the presence of Jean-Yves Le Drian, Defense Minister under the title «Inhale, you are saved».



A team collectif:



► Extracted from «La Nouvelle République.fr» -January 23, 2013- translated into English.

Aerorimac Project: administration of anti-ricinantibody by aerosol

Ricin is a toxin classified as a priority biological agent by the French Ministry of Defense. In the case of ricin's intoxication by pulmonary route, administration of an antidote in the deep lung should be a fast and efficient solution.

The team of Chief Medical Officer P. Thullier, French Armed Biomedical Research Institute (IRBA) has developed a highly effective antibody for neutralizing ricin. The development of an aerosol generator for administering this antibody post-intoxication directly into the lung by aerosol has a twofold challenge: a **technological challenge** for a generator targeting the deep lung and **biotechnological challenge** to aerosolize the antibody without altering its therapeutic properties. The AeroRiMac project began at the end of 2010, designed to meet these challenges and to develop an alveolar aerosol generator targeting the lung to deliver the anti-ricin antibody. It is supported by the French company **Diffusion Technique Française** (DTF Medical, nebulizer manufacturer, Saint-Etienne), through its research and development department **DTF-AERODrug** (Tours) located in the

premises of the **Centre for the Study of Lung Diseases** (Centre d'Etude des Pathologies Respiratoires- CEPR Inserm U1100/EA6305) located at the Faculty of Medicine of Tours. Inside the CEPR, team EA6305 (Aerosoltherapy and respiratory Bio-drugs) has an international reputation in the field of aerosol-drugs and has recently made pioneering works on aerosoltherapy of therapeutic antibodies (Maillet et al., 2008 and Maillet et al., 2011). This project brings together the firm SESAME (Chambray-Les-Tours), specializing in the evaluation of drug safety. Maturity of the project is scheduled for late 2013.

This project is financially supported by the General Delegation for Armaments (DGA), called Rapid, having a «dual» character, considering both military and civil applications to open future markets for small firms.

Detailed description of the project:

► **The first task of the project involves the establishment of a formulation of the anti-ricin antibodies (43RCA)** to allow its storage in powder form according to the specifications of the French army and extemporaneous reconstitution with a dedicated device, obtained from PCA (Army Forces Central Pharmacy), and with the design of a specific adapter. These steps of lyophilization and reconstitution are generative of constraints on antibodies that could lead to the formation of aggregates and / or decrease the affinity of the antibody. A buffer change was necessary to preserve the maximum integrity of the antibody, and we showed that the histidine buffer is the best candidate to limit the formation of aggregate 43RCA.

The second task is the study of the influence of mechanical parameters induced by aerosol generation of the antibody to ensure its physical integrity in aerosol form. Because of the small amount of available anti-ricin antibodies, using a human polyclonal IgG was required for the various developments and the validation of critical steps made with 43RCA. It has been shown from preliminary results that the addition of a surfactant, even at low concentrations (depending on coupled IgG concentration/ surfactants concentration), can limit the formation of aggregates.

Meanwhile, a vibrating mesh nebulizer has been developed (in partnership with Aerogen) to obtain an aerosol of which the diameter (VMD) is between 1 micron and 3 microns to reach the pulmonary alveoli and an aerosol storage chamber during the expiratory phase (patented), which provides a higher inhalable fraction of 80% and an «alveolar» fraction exceeding 20%. The ensemble is produced industrially in the project. The final task of the project, that will take place in 2013, will evaluate in-vitro and in-vivo performance of the nebulizer prototype developed in this study with anti-ricin antibody and pulmonary tolerance of the resulting formulation.

In the end, the AeroRiMac project should lead to the creation of an industrialized anti-ricin antibodies nebulizer prototype which will lead, ultimately, to systematically enable the immediate treatment of human lung exposure to ricin. ◀



AEROSOL THERAPY BY DTF MEDICAL



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