

## AP-HP and the start-up NeckEpur sign a valorization contract to improve drug management for intensive care patients.

July 28, 2023 - On June 9, 2023, Assistance Publique – Hôpitaux de Paris (AP-HP) signed an operating license agreement with NeckEpur. The contract covers the rights to use the patent of Professor Frédéric Baud (principal inventor) relating to a method for evaluating and optimizing the dose of drug administered to the intensive care patient.

NeckEpur is a company dedicated to the development of innovative solutions for blood purification. These solutions are based on a patented method of pharmacokinetic evaluation of the elimination of the free fraction of drugs under continuous extrarenal purification, developed by Professor Frédéric Baud in the Adult Multipurpose Medical Resuscitation Department of the Necker-Enfants Malades AP-HP hospital.

AP-HP's Clinical Research and Innovation Department has accompanied Professor Frédéric Baud since 2016 until the creation of the start-up in 2022 to perpetuate the know-how and continue to expand knowledge in the field.

NeckEpur aims to improve the medication management of patients in intensive care by monitoring the implementation of medical devices used in the extracorporeal circulation. A standardized and clinically validated protocol makes it possible to determine the degree of sequestration of drugs on hemodiafiltration membranes and thus to adjust the therapeutic dose by protocols tested *in vitro*, avoiding early underdosing, related to adsorption on the membranes or late overdose caused by the unexpected release of the drug. NeckEpur aims to reduce treatment failure and the risk of death.

In 2015, Professor Frédéric Baud, University Professor – Hospital Practitioner (PU-PH) in adult medical resuscitation undertook work at the Necker-Enfants Malades AP-HP hospital to study the sequestration of drugs by the filters of medical devices with extracorporeal circulation (MD-CEC) - continuous hemodiafiltration, ECMO, adsorbent columns, *etc.*. This work follows observations of therapeutic success in intoxicated patients in intensive care, characterized by clinical improvement without lowering plasma concentrations of the toxic under DM-CEC. This contrast suggested a decrease or even a disappearance of the free plasma concentration of drugs under DM-CEC: it is this free plasma concentration of drugs that has thus become the therapeutic target of NeckEpur, unlike all other methods.

Professor Baud has developed a model, classified *in vitro*, that reproduces in real scale continuous extrarenal purification (EERC) sessions and extends the modeling to other MD-CEC.

Research has confirmed that the sequestration of drug-free plasma concentrations by MD-CEC should be systematically studied for all drugs used in intensive care.

Clinical cases collected in adult intensive care and reported in pharmaco/materiovigilance confirm the relevance of the results of NeckEpur whose models had predicted failure or therapeutic difficulties.

The NeckEpur method requires multiple samples in the circuit, upstream and downstream, which make it possible to confirm or refute the sequestration of a drug on a filter and then to propose corrective measures in real conditions of use of the drugs. Twenty-five substances, mainly antibiotics and antifungals, were studied in support of the proof of concept. The results show significant sequestration

in 30% of the drugs studied and in the most intense sequestrations, the free form becomes undetectable, and is accompanied by the reappearance of the causative infection.

## References

1. Houze P, Baud FJ, Raphalen JH, Winchenne A, Moreira S, Gault P, et al. Continuous renal replacement therapy in the treatment of severe hyperkalemia: An in vitro study. *Int J Artif Organs*. 2020;43:87–93.
2. Baud FJ, Seif V, Houze P, Raphalen JH, Pilmis B, Carli P, et al. Elimination of three doses of gentamicin over three consecutive days using a polyacrylonitrile-derived filter: An in vitro assessment. *Int J Artif Organs*. 2021;44:641–50.
3. Baud FJ, Jullien V, Secretan PH, Houze P, Lamhaut L. Are we correctly treating invasive candidiasis under continuous renal replacement therapy with echinocandins? Preliminary in vitro assessment. *Anaesth Crit Care Pain Med*. 2020;:100640.
4. Baud FJ, Jetha-Jamal T, Vicca S, Raphalen J-H, Lamhaut L. Disposition of gentamicin and amikacin in extracorporeal membrane oxygenation using a heparin-coated filter: An in vitro assessment. *International Journal of Artificial Organs*. 2022;1:1–5.
5. Baud FJ, Houze P, Raphalen JH, Lamhaut L. Does Pharmacokinetics in the Central Compartment Evidence Routes of Elimination During Continuous Renal Replacement Therapy in Ex Vivo Model? *Crit Care Med*. 2020;48:e163–4.
6. Baud FJ, Jullien V, Abarou T, Pilmis B, Raphalen JH, Houze P, et al. Elimination of fluconazole during continuous renal replacement therapy. An in vitro assessment. *Int J Artif Organs*. 2021;44:453–64.
7. Baud FJ, Houze P, Raphalen JH, Winchenne A, Philippe P, Carli P, et al. Diafiltration flowrate is a determinant of the extent of adsorption of amikacin in renal replacement therapy using the ST150((R))-AN69 filter: An in vitro study. *Int J Artif Organs*. 2020;43:758–66.
8. Baud FJ, Houzé P, Carli P, Lamhaut L. Alteration of the pharmacokinetics of aminoglycosides by adsorption in a filter during continuous renal replacement therapy. An in vitro assessment. *Therapies*. 2021;76:415–24.
9. Raphalen JH, Marçais A, Parize P, Pilmis B, Lillo-Lelouet A, Lamhaut L, et al. Is caspofungin efficient to treat invasive candidiasis requiring continuous veno-venous hemofiltration? A case report. *Therapie*. 2021;76:512–5.
10. Le Ven J, Pellan C, Maulet V, Le Monnier A, Baud FJ. Elimination of cefotaxime using polysulfone and polyacrylonitrile-derived filters: An in vitro assessment. *Int J Artif Organs*. 2023;46:113–9.
11. Baud FJ, Houzé P, Raphalen J-H, Philippe P, Lamhaut L. Vancomycin Sequestration in ST Filters: An In Vitro Study. *Antibiotics (Basel)*. 2023;12:620.
12. Baud FJ, Jullien V, Desnos-Ollivier M, Lamhaut L, Lortholary O. Caspofungin sequestration in a polyacrylonitrile-derived filter. Increasing the dose does not mitigate sequestration. 2023. Soumis pour publication.

**About NeckEpur:** NeckEpur® is a company founded in March 2022 with the aim of providing medical device and pharmaceutical development manufacturers with a patented evaluation method to

measure drug sequestration by extracorporeal circulation circuits. Sequestration of drugs can lead to a decrease in their effectiveness, which can result in a prolonged stay in intensive care or even the death of the patient. NeckEpur© is therefore focused on the development of technologies and services to improve the care of patients in intensive care. The scope of NeckEpur© is innovative and a priority for regulatory agencies. <https://www.neckepur.com/>



**NECKEPUR**©

**Press contact: Dr Anne Villepelet-Castot: [annecharlottevillepelet@gmail.com](mailto:annecharlottevillepelet@gmail.com)**

**About** AP-HP: Europe's leading hospital and university centre (CHU), AP-HP and its 38 hospitals are organised into six university hospital groups (AP-HP. Centre - Paris Cité University; AP-HP. Sorbonne University; AP-HP. Nord - Université Paris Cité; AP-HP. Paris Saclay University; AP-HP. Henri Mondor University Hospitals and AP-HP. University Hospitals Paris Seine-Saint-Denis) and are structured around five universities in the Paris region. Closely linked to major research organizations, AP-HP has eight world-class university hospital institutes (ICM, ICAN, IMAGINE, FOrEoSIGHT, PROMETHEUS, InovAND, Re-Connect, THEMA) and the largest French health data warehouse (DHS). A major player in applied research and health innovation, AP-HP holds a portfolio of 650 active patents, its clinician researchers sign more than 10,000 scientific publications each year and more than 4,000 research projects are now under development, all promoters combined. In 2020, AP-HP obtained the Institut Carnot label, which rewards the quality of partnership research: Carnot@AP-HP offers industrial players solutions in applied and clinical research in the field of health. In 2015, AP-HP also created the AP-HP Foundation, which acts in direct contact with caregivers to support the organization of care, hospital staff and research within AP-HP. <http://www.aphp.fr>



**Press contact:**

AP-HP Press Office: 01 40 27 37 22 - [service.presse@aphp.fr](mailto:service.presse@aphp.fr)