France's Mediator° trial reveals a cosy relationship between representatives of the French drug regulatory agency and an influential company

ABSTRACT

● **The court has given its verdict in the historic criminal trial involving the Mediator° (*benfluorex*) disaster, which was held in Paris from September 2019 to September 2020, ten years after this drug was withdrawn from the market in France. The company, Servier, and the French drug regulatory agency were both found guilty.**

● **The trial revealed how representatives of the agency, external experts charged with drug evaluation, and the company were constantly trying to come to a consensus, leading to a delay in the decision to withdraw Mediator° from the market.**

● **Some of the external experts, whose opinion was paramount, had a close relationship with the pharmaceutical industry. Several of them shared certain characteristics: naivety and a cavalier attitude towards conflicts of interest, coupled with inflated self-esteem leading to an unrealistic belief that they were immune from conflicts of interest.**

● **Some external experts also shared the pharmaceutical industry's overly positive view of drugs in general. As regards Mediator°, having failed to make the appropriate comparisons, most experts were left with an incomplete view of the drug's harm-benefit balance. Nor did they take a sufficiently critical approach to the company's data.**

● **These factors contributed to the unjustified, continued marketing of Mediator° for more than thirty years, and the resulting harms to patients.**

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Some key dates in the Mediator° disaster

1976. The company, Servier, markets the drug *benfluorex* in France under the brand name Mediator°. The drug's principal action is appetite suppression, but it is mainly presented as an antidiabetic and lipid-lowering drug.

1977. The French journal *Pratiques* questions the efficacy of Mediator° and points out its similarity to Ponderal°, another fenfluramine appetite suppressant manufactured by Servier. One year later, Henri Pradal carries out a similar analysis in his *Dictionnaire critique des médicaments*.

1997. Worldwide market withdrawal of Servier's other fenfluramine appetite suppressants, because they cause pulmonary arterial hypertension (PAH) and heart valve disease.

1997. *Prescrire* observes that "*there is currently no basis for treating noninsulin-dependent diabetics with benfluorex. The French health authorities should reconsider their decision to license and reimburse this product*".

1999. The first reported cases of PAH and heart valve disease associated with Mediator°.

2003, 2005, 2006, 2008 and 2009. *Prescrire* publishes reminders of the risks of PAH and heart valve disease linked to *benfluorex*, supported by data.

2009. Market withdrawal of Mediator° in France, following a pharmacovigilance safety alert.

2010. Publication of the book *"Mediator 150 mg, combien de morts?"* (Mediator 150 mg, how many deaths?) (Irène Frachon, éditions Dialogues). Servier initially obtained a court order censoring the subtitle "How many deaths?"

2011. A "drug safety" law is passed, in response to the Mediator° disaster. Among the measures, a new drug regulatory agency, ANSM, replaced the previous one.

2019-2021. The criminal trial relating to the disaster. An appeal will be heard, in 2022 at the earliest.

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