



## 1. Adverse effect vs. side effect

François Noël, September 2013

**Side effect:** this is an effect different from the primary one responsible for the drug's therapeutic action and use. Thus, a side effect may be beneficial or neutral and is not necessarily adverse or undesirable ("unwanted side effect"). According to this interpretation, one may cite the document *Clinical Safety Management: Definitions and Standards for Expedited Reporting – E2A*, recommended for adoption by regulatory authorities in the European Community, Japan, and the United States (International Conference on Harmonisation – ICH). Indeed, this document (II.A.2.) clearly states that "*the old term 'side effect' has been used in various ways in the past, usually to describe negative (unfavorable) effects, but also positive (favorable) effects. It is recommended that this term no longer be used and, in particular, that it not be regarded as synonymous with adverse reaction.*"

It can be noted that there may be controversy regarding the definition of *side effect*, but not regarding the need to abandon this term, as will be shown below. In the *Textbook of Clinical Pharmacology and Therapeutics* (ed. Grahame-Smith & Aronson, 3rd edition – Guanabara Koogan), it is stated that "*an adverse effect refers to an unwanted effect of a drug. Adverse effects may result from toxic effects or side effects. A toxic effect is an adverse effect that arises as a consequence of intensification of the same pharmacological effect responsible for the drug's therapeutic action; therefore, it is a dose-related effect. A side effect refers to an adverse effect that arises through some pharmacological action distinct from that producing the therapeutic effect (these effects may or may not be dose-related).*" In any case, this term should be avoided, as recommended by the same authors: "*Because dose-related side effects may also be regarded as toxic effects, it is more appropriate to avoid the terms 'toxic effects' and 'side effects' and instead use the term 'adverse effects', which encompasses all types of unwanted effects.*"

Accordingly, we should use the term **ADVERSE EFFECT** (or "undesirable effect"), consistent with the term **ADVERSE DRUG REACTION (ADR)**, which is well established in pharmacovigilance ("*Any response to a medicinal product that is harmful and unintended and occurs at doses normally used in humans for the prophylaxis, diagnosis, or treatment of disease, or for the modification of a physiological function*"- ANVISA, Resolution RDC No. 140, May 29, 2003). It should be noted that this definition is fully consistent with that given by the World Health Organization ([the importance of pharmacovigilance: safety monitoring of medicinal products](#)).