

Appendix S1

SUPPLEMENTAL METHODS

The 2x2 table below explains what the reporting odds ratio (ROR) represents. The odds of an event occurring is defined as the likelihood that an event will occur, expressed as a proportion of the likelihood that any other event in the World Health Organization (WHO) database will occur. The ROR represents the odds that an event will occur during a specified biologic (product X), compared with the odds of the event occurring during any other drug in the WHO database (all other products). C "all other products" can be adapted according to the research question. We have performed a disproportionality analysis with "all other products" as reference group. The reference group "all other products" contains every drug in the WHO database. Since spontaneous safety reports are made only when an adverse drug reaction occurs, there is no comparison with biologic or other drug recipients with no adverse drug reactions. Normally, an odds ratio represents the chance of an outcome compared with not having that outcome, since the latter is not possible in the WHO database "all other events" serve as a comparison. Also comparison to the "unexposed" is not possible therefore "all other products (drugs)" serve as a comparison.

The following equation is used by the WHO to calculate reporting odds ratios: $ROR = \frac{Cxy * (C - Cx - Cy + Cxy)}{(Cy - Cxy) * (Cx - Cxy)}$ $= \frac{a * ((a + b + c + d) - (a+b) - (a+c) + a)}{((a + c) - a) * ((a + b) - a)}$ $= \frac{a * (d + a)}{c * b} = \frac{a * d}{c * b}$. An association is defined as a minimum of 3 ICSRs, and a lower limit of the 95% confidence interval of the reporting odds ratio >1.

	Event	All other events
Product X	a	b
All other products	c	d

Product X (index group): The selected biologic.

Event: Bacterial skin infection or *Herpesviridae* infection.

All other events: All other adverse drug reactions in the database.

All other products (reference group): All other drugs in the database.

$Cxy = a =$ (number of reports for the drug-event combination = Nobserved)

$Cx = a + b =$ (number of reports for the drug = Ndrug)

$Cy = a + c =$ (number of reports for the event = Nreaction)

$C = a + b + c + d =$ (number of reports in total = Ntotal)