



Universidade de São Paulo
Faculdade de Ciências Farmacêuticas
Departamento de Farmácia

INTRODUÇÃO A METROLOGIA: AVALIAÇÃO DA INCERTEZA DE MEDIÇÃO

FBF5833 – Qualidade por Design Analítica
(AQbD) Aplicado às Análises Farmacêuticas

Prof. Dr. Felipe Rebello Lourenço

INTRODUÇÃO



Resultados analíticos...

- Importância em diversas áreas
- Preocupação com sua qualidade
- Apesar dos esforços

...Incerteza de medição!

CONCEITOS E DEFINIÇÕES



Princípios do GUM...

- Incerteza padrão (u)
- Fator de abrangência (k)
- Incerteza expandida ($U = k \times u$)

...intervalo com 95% de confiança!

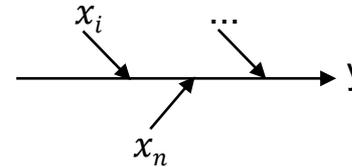
ETAPAS PARA OBTER "MU"



Especificar
mensurando

$$y = f(x_i \dots x_n)$$

Identificar das fontes de
incerteza



Quantificar e padronizar das
incertezas

$$u_{x_i} \dots u_{x_n}$$

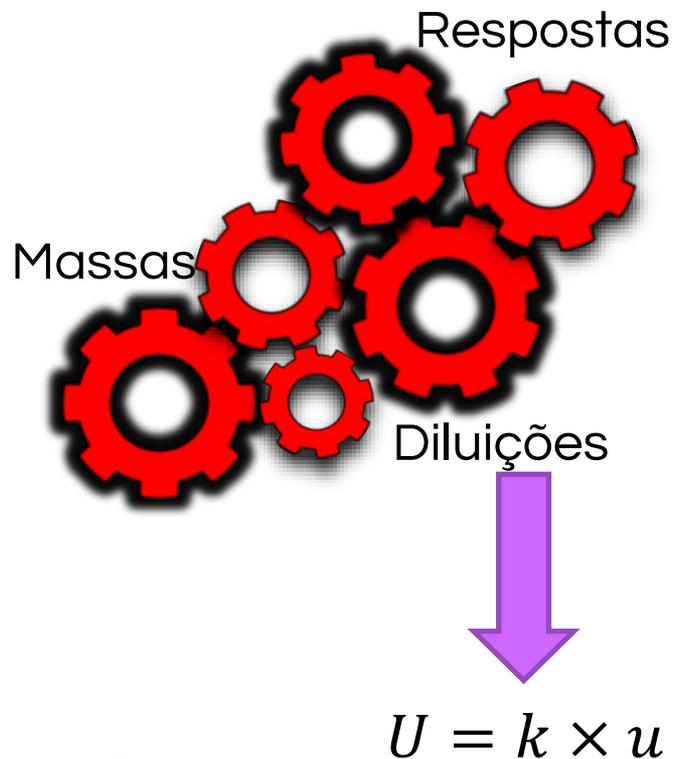
Calcular incertezas
combinadas e expandida

$$U_y = k \times u_y$$

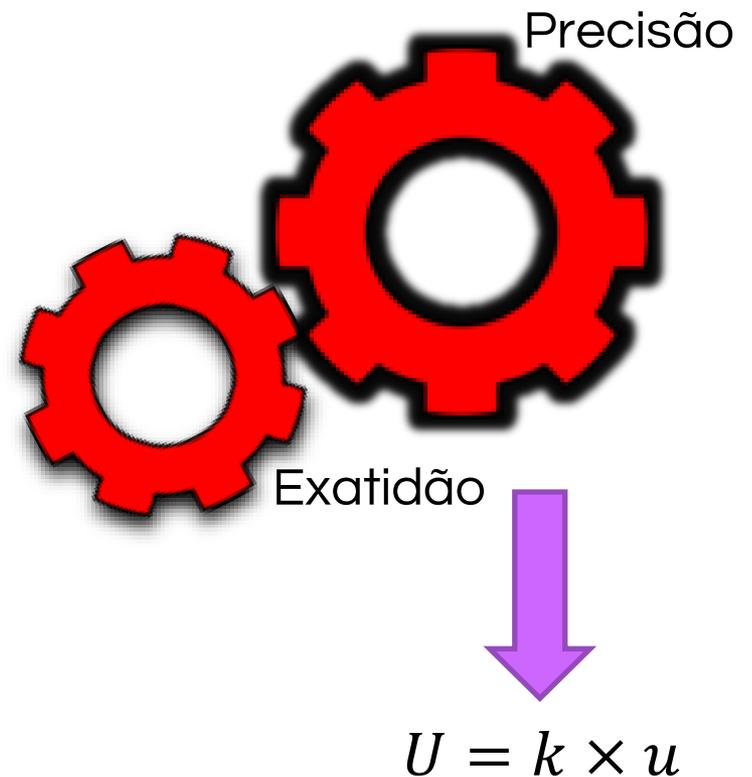
MÉTODOS PARA OBTER "MU"



Abordagem *bottom-up*...



Abordagem *top-down*...



LEI DA PROPAGAÇÃO DAS INCERTEZAS



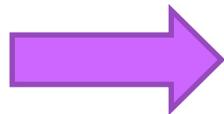
$$y = f(x_1, x_2)$$



$$u_y = \sqrt{u_{x_1}^2 \left(\frac{\partial y}{\partial x_1}\right)^2 + u_{x_2}^2 \left(\frac{\partial y}{\partial x_2}\right)^2 + u_{x_1} u_{x_2} \left(\frac{\partial y}{\partial x_1}\right) \left(\frac{\partial y}{\partial x_2}\right) r_{12}}$$

A purple arrow points from the r_{12} term in the denominator to the number 0 on the right side of the equation.

Se $r_{12} = 0$



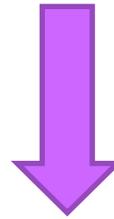
$$u_y = \sqrt{u_{x_1}^2 \left(\frac{\partial y}{\partial x_1}\right)^2 + u_{x_2}^2 \left(\frac{\partial y}{\partial x_2}\right)^2}$$

LEI DA PROPAGAÇÃO DAS INCERTEZAS



Regra da soma / subtração

$$y = x_1 + x_2 - x_3$$



$$u_y = \sqrt{u_{x_1}^2 \left(\frac{\partial y}{\partial x_1}\right)^2 + u_{x_2}^2 \left(\frac{\partial y}{\partial x_2}\right)^2 + u_{x_3}^2 \left(\frac{\partial y}{\partial x_3}\right)^2}$$

+1 +1 -1

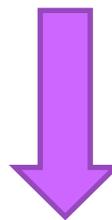
$$u_y = \sqrt{u_{x_1}^2 + u_{x_2}^2 + u_{x_3}^2}$$

LEI DA PROPAGAÇÃO DAS INCERTEZAS



Regra da multiplicação / divisão

$$y = \frac{x_1 \times x_2}{x_3}$$



$$\frac{u_y}{y} = \sqrt{u_{x_1}^2 \left(\frac{\partial y}{\partial x_1}\right)^2 + u_{x_2}^2 \left(\frac{\partial y}{\partial x_2}\right)^2 + u_{x_3}^2 \left(\frac{\partial y}{\partial x_3}\right)^2}$$

Diagram illustrating the partial derivatives for the multiplication/division rule. Purple arrows point from the partial derivative terms to their simplified forms: $\frac{\partial y}{\partial x_1} \rightarrow \frac{x_2}{x_3}$, $\frac{\partial y}{\partial x_2} \rightarrow \frac{x_1}{x_3}$, and $\frac{\partial y}{\partial x_3} \rightarrow -\frac{x_1 \times x_2}{x_3^2}$. A purple line underlines the y in the denominator of the left side of the equation.

$$u_y = y \sqrt{\left(\frac{u_{x_1}}{x_1}\right)^2 + \left(\frac{u_{x_2}}{x_2}\right)^2 + \left(\frac{u_{x_3}}{x_3}\right)^2}$$

MÉTODO DA PLANILHA DE KRAGTEN

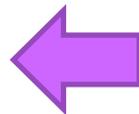


$$y = f(x_1, x_2, x_3)$$

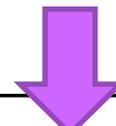
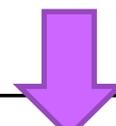
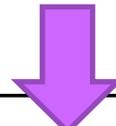
	u_{x_1}	u_{x_2}	u_{x_3}
x_1	$x_1 + u_{x_1}$	x_1	x_1
x_2	x_2	$x_2 + u_{x_2}$	x_2
x_3	x_3	x_3	$x_3 + u_{x_3}$

y	y_{x_1}	y_{x_2}	y_{x_3}
-----	-----------	-----------	-----------

$$u_y = \sqrt{\sum (y - y_{x_i})^2}$$

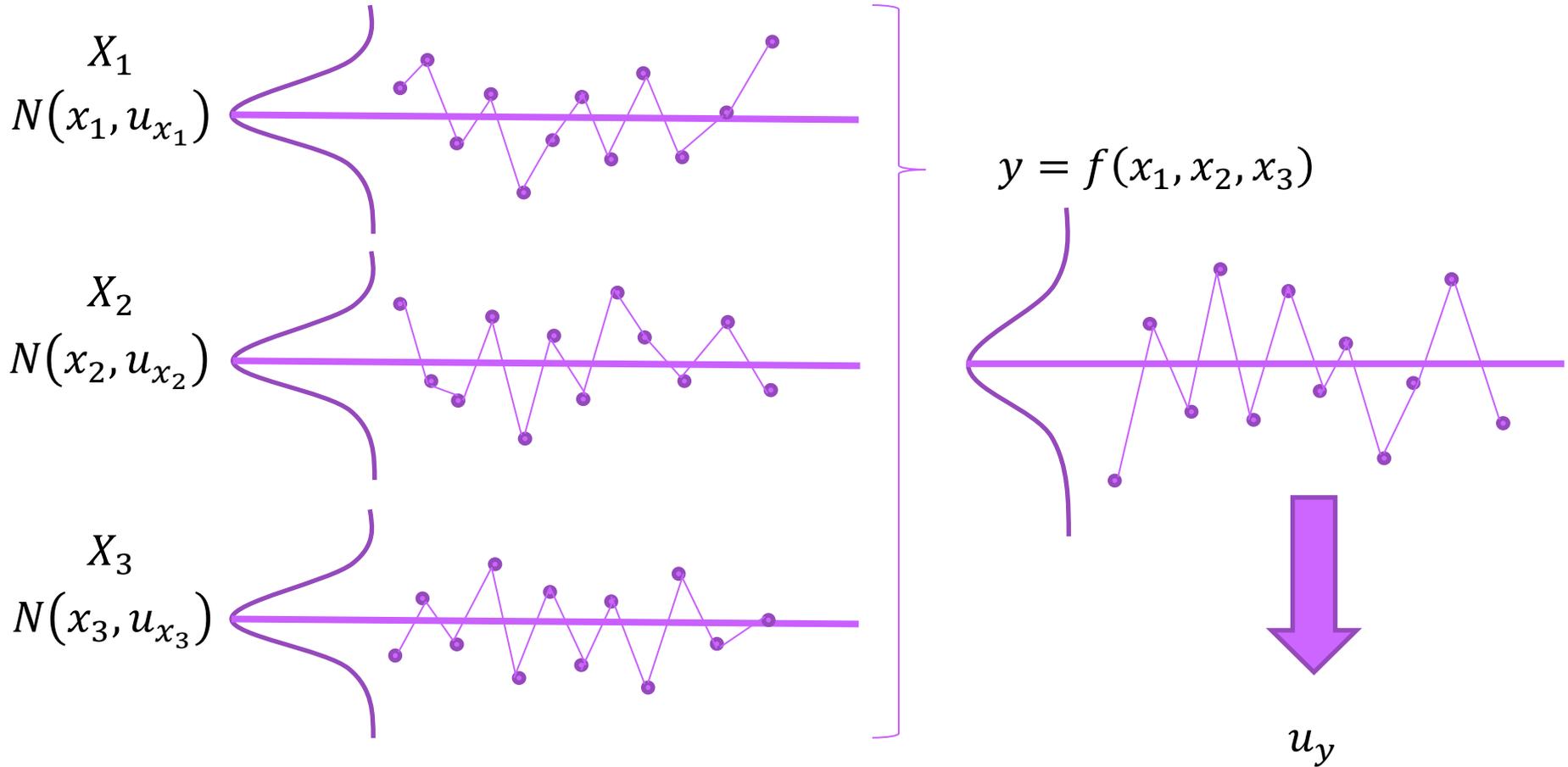


$(y - y_{x_1})^2$	$(y - y_{x_2})^2$	$(y - y_{x_3})^2$
-------------------	-------------------	-------------------

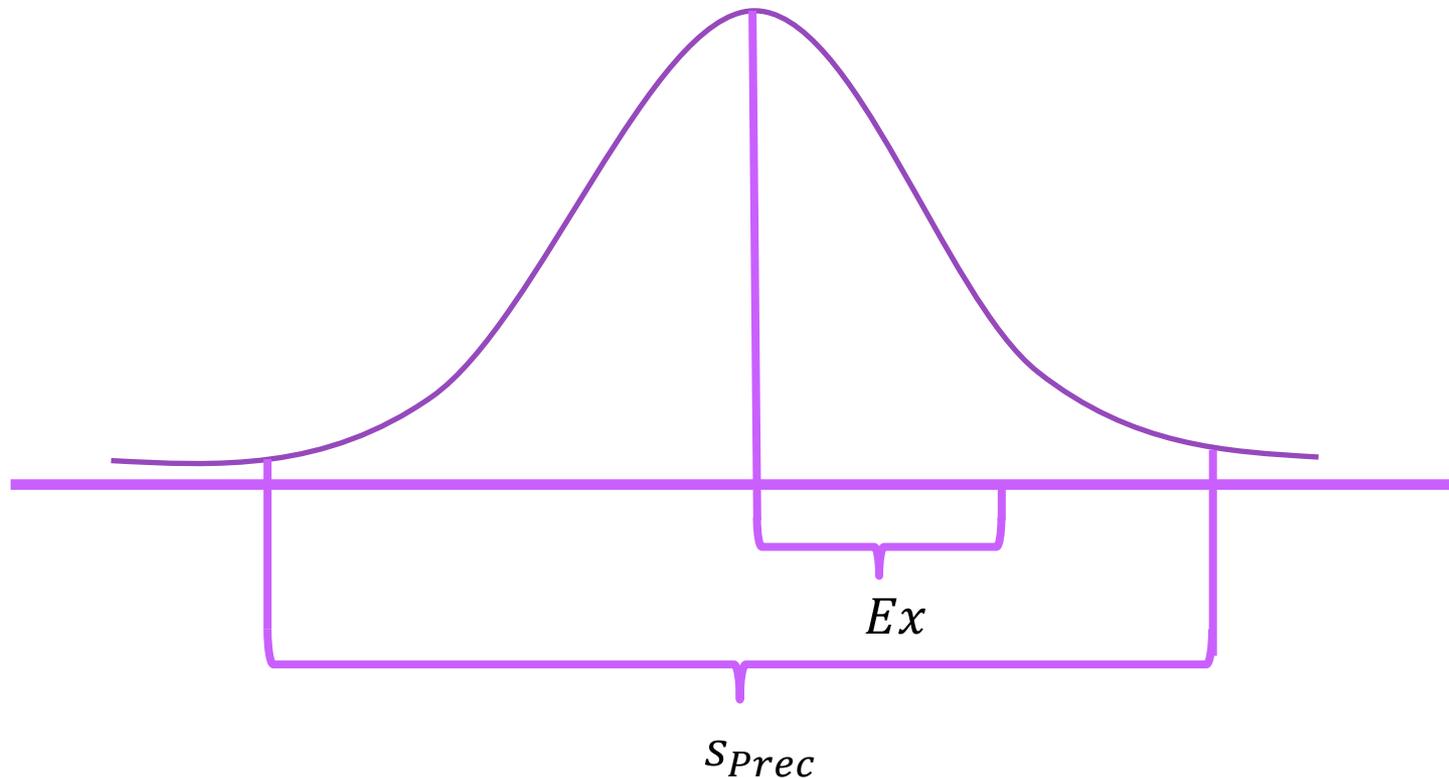


$$u_y = \sqrt{u_{x_1}^2 \left(\frac{\partial y}{\partial x_1}\right)^2 + u_{x_2}^2 \left(\frac{\partial y}{\partial x_2}\right)^2 + u_{x_3}^2 \left(\frac{\partial y}{\partial x_3}\right)^2}$$

SIMULAÇÕES DE MONTE CARLO

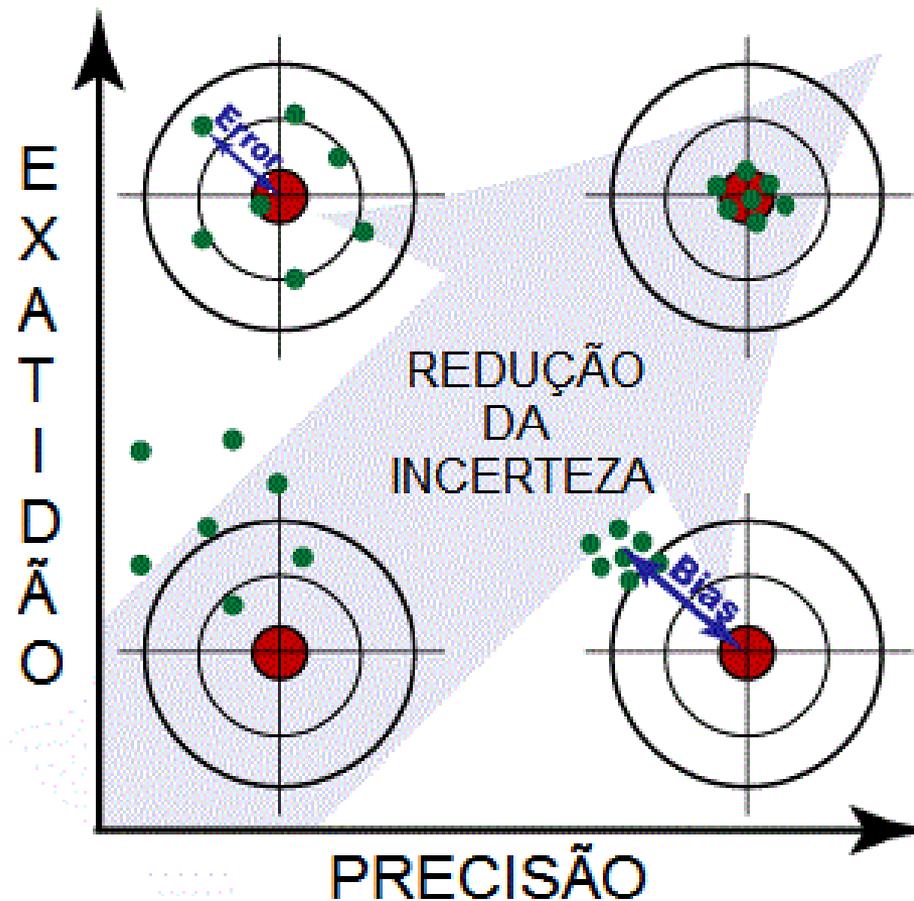


VALIDAÇÃO DE MÉTODOS



$$u = \sqrt{(1 - Ex)^2 + S_{Prec}^2}$$

VALIDAÇÃO DE MÉTODOS



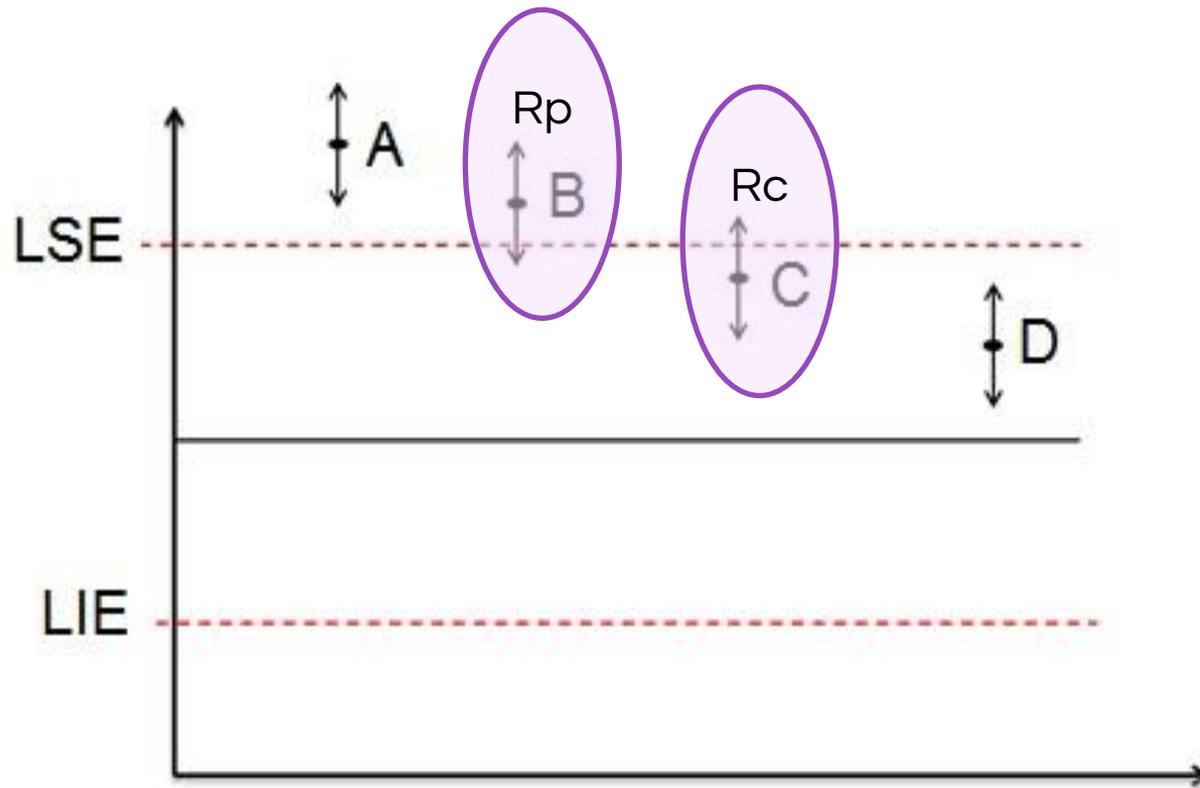
APLICAÇÃO DA INCERTEZA: CONFORMIDADE



Estimativa dos riscos...

- Produtor x Consumidor
- Particular x Total
- Global x Específico

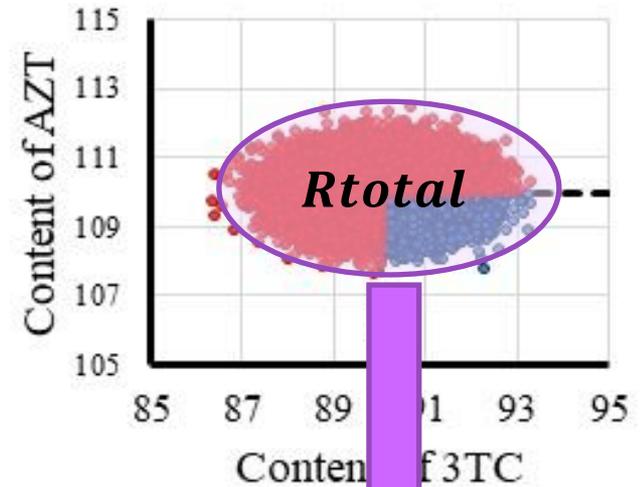
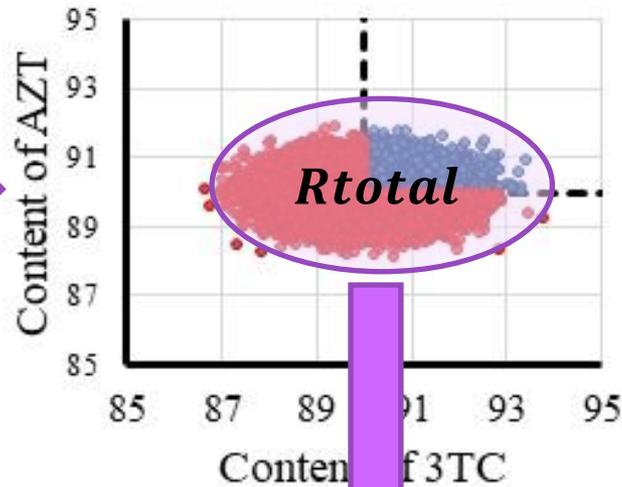
ESTIMATIVA DE RISCOS: PRODUTOR x CONSUMIDOR



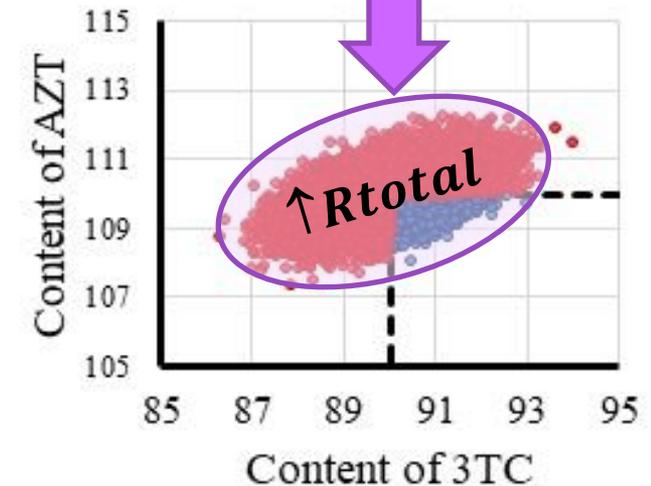
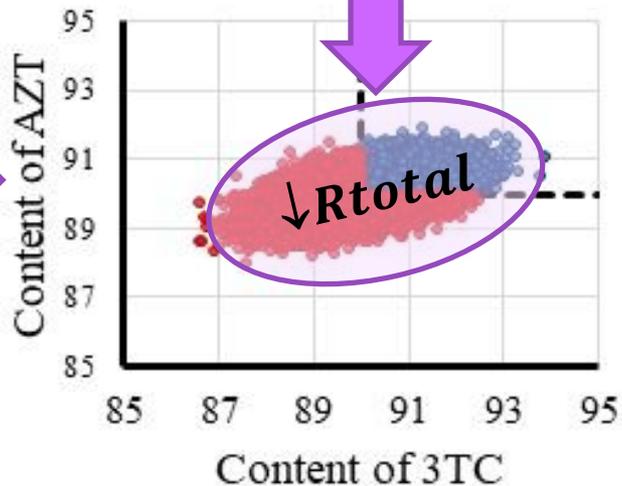
ESTIMATIVA DE RISCOS: PARTICULAR x TOTAL



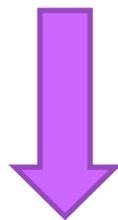
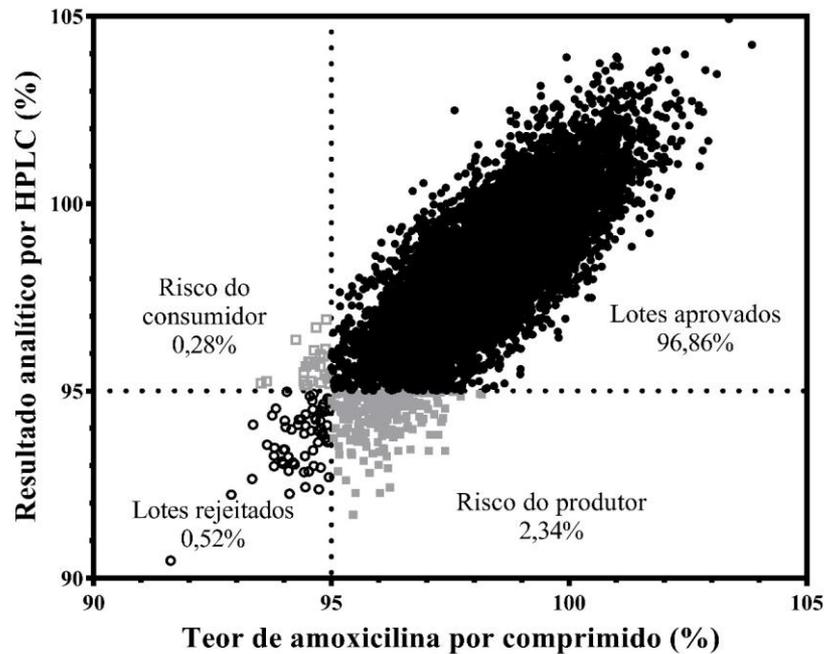
$$r = 0$$



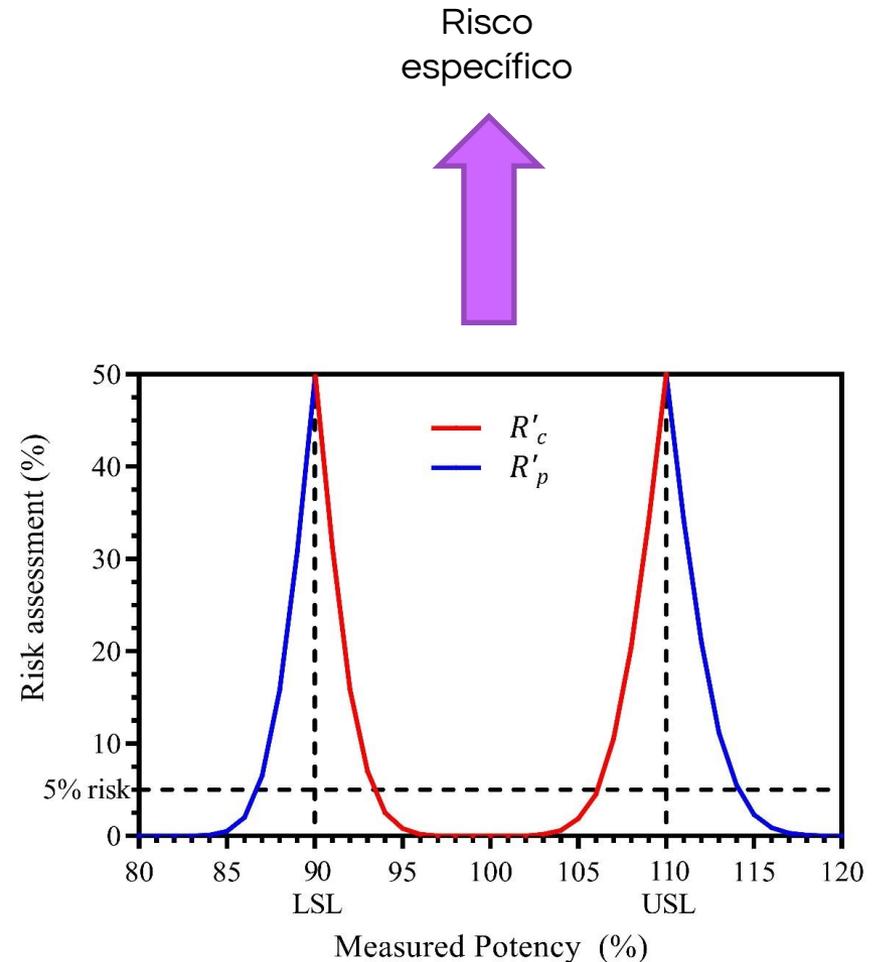
$$r \neq 0$$



ESTIMATIVA DE RISCOS: GLOBAL x ESPECÍFICO



Risco
Global



REFERÊNCIAS



- Ellison & Barwick, 2008.
- Ellison & Williams, 2012.
- Gadrich & Bashkansky, 2016.
- Galvão, Saviano & Lourenço, 2016.
- Ghisleni, Okamoto, Amaral, Lourenço & Pinto, 2014.
- ISO/GUM, 2008.
- ISO/GUM – Supplement 1, 2008.
- Kuselman, Pennechi, Silva & Hibbert, 2017.
- Lourenço, 2013.
- Lourenço, Botelho & Pinto, 2012.
- Lourenço, Kaneko & Pinto, 2005.
- Lourenço, Kaneko & Pinto, 2007.
- Mueller, 2002.
- Ostronoff & Lourenço, 2015.
- Saviano & Lourenço, (Talanta) 2018.
- Saviano & Lourenço, (Measurement) 2018.
- Saviano, Francisco & Lourenço, 2014.
- Separovic, Saviano & Lourenço, 2018.
- Traple, Saviano, Francisco & Lourenço, 2014.
- Williams, 1998.



Universidade de São Paulo
Faculdade de Ciências Farmacêuticas
Departamento de Farmácia

OBRIGADO!

Prof. Dr. Felipe Rebello Lourenço