**Supplementary Appendix**

**Supplementary Table 1**. **Analytical parameters and performances of the three methods used for IND, GLY and MF**

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| --- | --- | --- | --- | --- | --- |
| **Compound** | **Analytical conditions -** | **Calibration range** | **MS Parameters** | **Bias (%)a** | **Precision (%)b** |
| Indacaterol | Sample processing solid phase extraction on Oasis Mixed mode (10 mg, 30 µm) cartridge using a sample volume of 200 µL.Separation: Acquity UPLC® BEH C18 1.7µM at 40°C and using 0.1% formic acid in water as mobile phase A, acetonitrile as mobile phase B and operating at a gradient with an initial flow rate of 0.750 mL/min.A triple quadrupole mass spectrometer (API 6500) equipped with a turbo ion spray source is used for detection in positive ion mode. Quantification is based on multiple reaction monitoring (MRM) of the transitions of m/z 392.9 – 173.2  | 5.00 to 5000 pg/mLA linear calibration curve with a 1/x2 weighting | Curtain gas 50 units GS1 (nebulizing gas, N2) 50 units; GS2 (desolvation gas, N2) 65 unitsIon spray voltage 5000 V; Source Temperature: 500°CDeclustering Potential 50 VCollision Energy 30 VCollision exitPotential 20 V | 1.9 – 2.4 | 0.3 – 2.4  |
| Glycopyrronium | Sample processing: solid phase extraction on Oasis weak cationic ion exchange (10 mg, 30 µm) cartridge using a sample volume of 200 µL.Separation: ACQUITY UPLC BEH C18 analytical column at 45°C and using 0.1% formic acid in water as (mobile phase A) and acetonitrile as (mobile phase B) operating at a gradient with a flow rate of 0.750 mL/min. Total run time 3 min.Instrument: triple quadrupole 6500 mass spectrometer equipped with a turbo ion spray source used for detection in positive mode Quantification: multiple reaction monitoring (MRM) of the transitions of m/z 318.0 – 116.1. | 1.00 to 1000 pg/mLA linear calibration curve with a 1/x2 weighting | Curtain gas 35 units; GS1 (nebulizing gas, N2) 50 units; GS2 (desolvation gas, N2) 65 units;Ion spray voltage 5000 V; Source Temperature: 500°CDeclustering Potential 100 VCollision Energy 35 VCollision exitPotential 20 V | -4.8 – 4.7 | 1.7 – 3.7 |
| Mometasone furoate | Sample processing: liquid-liquid extraction using a sample volume of 800 µL plasmaSeparation: Acquity UPLC BEH C18 column at 60°C, using 0.05% ammonia in water as (mobile phase A), and acetonitrile (mobile phase B), operating at a gradient with a flow rate of 1.00 mL/min. Total run time 3.5 min.Instrument: triple quaduprole 6500 mass spectrometer equipped with a turbo ion spray source is used for detection in positive ion mode. Quantification: MRM using transitions of m/z 521.1 → 355.2  | 0.250 - 100 pg/mLA linear calibration curve with a 1/x2 weighting | Curtain gas 25 units; GS1 (nebulizing gas, N2) 65 units; GS2 (desolvation gas, N2) 60 units;Ion spray voltage 3500 kV; Declustering Potential 30 VCollision Energy 21 VCollision exitPotential 10 V | 3.1 – 4.0 | 0.5 – 5.9 |

aData obtained during the three validation runs

bData obtained during the three validation runs