Electronic supplementary material

ESM Table 2 Consensus among four leading European clamp groups involved in glucose clamp studies of long-acting insulin analogues after participation in the expert meeting

Study design
1. The duration of action of an insulin preparation is most reliably measured in type 1 diabetic patients, i.e. subjects without endogenous insulin secretion
2. One drawback of using a continuous i.v. insulin infusion throughout the clamp, to suppress endogenous insulin secretion, is the metabolic effect of the infused insulin, which may result in overestimation of the duration of action of the study insulin
3. Study participants' insulin sensitivity, and thus the resulting time–action profile of the study insulin, is influenced by a number of factors, such as the time of day of study insulin injection, the duration of fasting, physical activity and any residual activity of pre-study insulin injections
4. Ideally, the end of the clamp is defined as the time after study insulin administration at which the glucose concentration reaches >11.1 mmol/l (200 mg/dl), without setting a time limit for clamp duration
5. The recommended clamp glucose target when studying diabetic patients is 5.6 mmol/l (100 mg/dl); healthy volunteers should be clamped at a sub-fasting glucose level
6. The duration of action of an insulin preparation is dose-dependent and the study insulin dose should be a clinically relevant dose, reflecting the mean basal insulin requirement of the study population
Outcome measures
1. GIR-AUC is the most robust outcome measure; GIR_{max} and t_{GIRmax} should be regarded as secondary outcomes as they are derived from smoothed GIR curves
2. Any definition of both onset and end of action is arbitrary
3. Onset of action is not a solid PD endpoint, especially for long-acting insulin analogues
4. The end of action of an insulin preparation is defined as the time after study insulin administration at which the glucose concentration reaches >8.3 mmol/l (150 mg/dl)
Statistical methods
1. When averaging individual time–action profiles to produce a single mean curve, the GIRs of the study participants in whom end of action occurred before the end of study (by definition, GIR = 0 mmol kg^{-1} min^{-1}) should be included in the calculation of the mean curve
2. GIR-AUC should be calculated from unsmoothed, raw data

Mode of reporting
1. Clamp quality should be reported both as the mean and the SD of the glucose concentrations of the individual clamp procedures, and as the mean and SD of the SDs of the glucose concentrations of the individual clamp procedures
2. When clamping healthy volunteers or patients with type 2 diabetes, the absence of C-peptide stimulation should be demonstrated
3. Duration of action should be reported both as onset of action to end of action, and as the time of study insulin injection to end of action
4. Both mean and individual time–action profiles should be reported
5. When averaging individual time–action profiles to produce a single mean curve, the number of study participants that remain to constitute the mean curve should be mentioned on the *x*-axis