Evaluation of the safety and usability of FlexPro® 30 mg/3 mL for the delivery of Norditropin® in patients requiring growth hormone therapy

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Disclosures: GF and MQ are employees of and stock/shareholders in Novo Nordisk.
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Introduction

- FlexPro® 30 mg/3 mL (Novo Nordisk A/S, Denmark) is a pre-filled ready-to-use pen-injector intended as a delivery system for liquid Norditropin® (recombinant human growth hormone [GH], Novo Nordisk A/S, Denmark) for patients requiring GH therapy. FlexPro® 30 mg/3 mL is not yet approved for use by health authorities but has been submitted to the FDA and is currently under review.
- GH therapy has been proven effective in patients with GH deficiency (GHD), including adult GHD, Turner syndrome (TS), Noonan syndrome (NS) and short children born small for gestational age (SGA) (Harris *et al. Paediatr Drugs* 2004;6:93–106; Appelman-Dijkstra *et al. Eur J Endocrinol* 2013;169:R1–14).
- This summative usability test assessed the safety and usability of critical frequently used, and primary-operating functions of FlexPro® 30 mg/3 mL, and validated the instructions for use (IFU) and instructional video in the intended user groups.

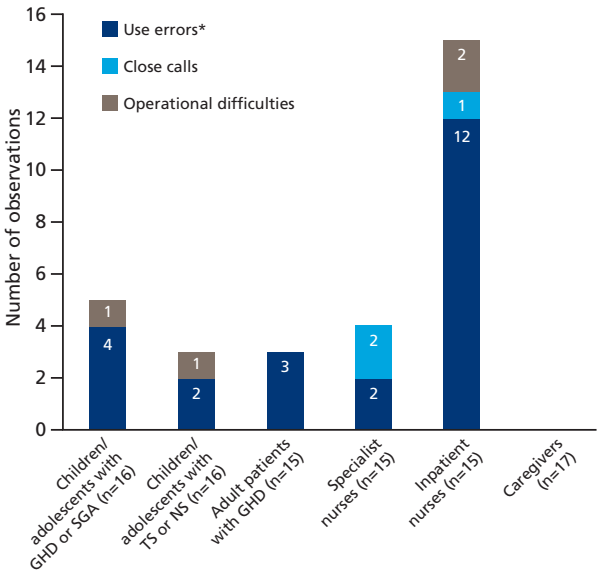
Methods

- Children and adolescents aged 10–17 years with GHD, SGA, TS or NS (approved indication in the USA, Switzerland, Israel, South Korea and the Philippines), adult patients aged ≥18 years with GHD, caregivers of patients with GHD, SGA, TS or NS and specialist and inpatient nurses were enrolled in accordance with FDA Human Factors Engineering (HFE) guidelines.
- All participants, except inpatient nurses, received training in using FlexPro® 30 mg/3 mL to ensure the pen-injector can be used safely and effectively. Inpatient nurses are expected to use products without specific training.
- All enrolled participants were tested on normal use (of new pen-injector), end-of-content use (almost depleted pen-injector), and IFU comprehension.
- Injections were performed into a foam cushion.
- Use errors, close calls (nearly committing a use error), operational difficulties and abnormal uses were recorded and evaluated by trained observers based on participants' subjective feedback.
- All participants completed a post-test questionnaire related to overall experience using FlexPro® 30 mg/3 mL, the IFU, instructional video and training materials (21-item; 7-point scale: 1=strongly disagree; 7=strongly agree).

Results

- Overall, 94 participants underwent evaluation, of which 74.5% were female.
- Baseline demographics are provided in Table 1. On average (range), specialist and inpatient nurses had 16 (2–38) years of experience as healthcare practitioners, while specialist nurses had 9 (1–23) years of experience training and/or managing patients requiring GH.
- 81% of participants completed both handling tests and the IFU comprehension test without use errors.
- No task failures, potentially serious (potential association with a serious adverse event) or non-serious (potential association with a non-serious adverse event) errors were recorded.
- In total, 23 use errors (no potential for harm, Figure 1) were committed by 19% of participants (n=18). The majority of use errors were related to participants not checking the flow on a new pen injector (17 errors by 12 participants) (Figure 2).
  - >50% of use errors (n=12) were committed by eight untrained inpatient nurses.
  - There was no major difference in the number of use errors recorded between pen-experienced and pen-naïve participants.
  - No use errors were recorded when patients were able to refer to the IFU or instructional video.
- Three close calls and four operational difficulties were reported by three and four participants, respectively (Figure 1). Operational difficulties were related to removing the needle without re-capping.

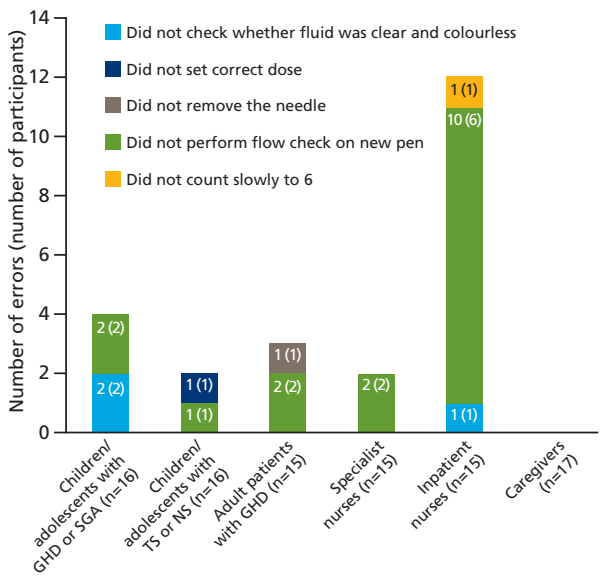
Figure 1 Overall observations by group.



*Use errors related to handling with no potential for harm. GHD, growth hormone deficiency; SGA, small for gestational age; TS, Turner syndrome; NS, Noonan syndrome.

- All participants correctly interpreted three out of four IFU excerpts, and provided positive responses for their overall experience with FlexPro® 30 mg/3 mL (mean ratings between 6 and 7). Mean (range) ratings of 6.7 (4–7) and 6.7 (5–7) were recorded for 'FlexPro® was simple to use', and 'FlexPro® was easy to learn to use', respectively. Ten participants did not interpret the 'check flow' excerpt (ensure GH can flow through pen and needle) correctly.
- Mean ratings between 6 and 7 were also recorded for the evaluation of the IFU and instructional video. The IFU and instructional video (mean rating [range]) showed information clearly and effectively (6.7 [5–7] and 6.8 [5–7], respectively), and were easy to understand (6.7 [5–7] and 6.8 [6–7], respectively).
- This usability test was associated with some limitations: no blinding took place, the test was carried out in a controlled setting (not in the participant's home or natural environment) and injections were performed into a foam cushion and not the participant's own body, leading to different tactile feedback.

Figure 2 Use errors related to handling by group. Data are number of errors (number of participants).



GHD, growth hormone deficiency; SGA, small for gestational age; TS, Turner syndrome; NS, Noonan syndrome.

Table 1 Baseline demographics and patient characteristics.

	Average age, years (range)	Gender, male/female	Average length of diagnosis, months (range)	Pen-experienced/ pen-naïve	Average length of experience using pen injectors*, months (range)
Children/adolescents with GHD or SGA (n=16)	13 (10–16)	11/5	65 (19–180)	8/8	42 (8–96)
Children/adolescents with TS or NS (n=16)	12 (10–17)	1/15	78 (14–156)	10/6	66 (11–156)
Adult patients with GHD (n=15)	45 (18–76)	7/8	104 (12–264)	9/6	47 (6–156)
Specialist nurses (n=15)	40 (24–60)	1/14	N/A	N/A	N/A
Inpatient nurses (n=15)	43 (30–59)	1/14	N/A	N/A	N/A
Caregivers (n=17)	40 (24–52)	3/14	72 (8–180)	9/8	62 (6–120)

*Excluding pen-naïve participants (including nurses and caregivers). GHD, growth hormone deficiency; SGA, small for gestational age; TS, Turner syndrome; NS, Noonan syndrome

Conclusions

- Overall, participants reported positive experiences with FlexPro® 30 mg/3 mL, the IFU and instructional video.
- No task failures, potentially serious or non-serious use errors were observed.
- The majority (81%) of participants committed no errors in the handling scenarios or IFU interpretation scenarios. Untrained participants committed more handling use errors (no potential for harm) than trained participants.
- Positive experiences with GH injection devices may improve user adherence and clinical outcomes.

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