This document is a note from the sponsor which was sent as part of their response to the factual check of the External Assessment Centre assessment report. It was inadvertently left out of the printed packs and should be read with the Sponsor's factual check of the External Assessment Centre assessment report (see Tab 6 of the printed pack). The EAC have responded to the points raised at the end of the factual check table included in Tab 6.

Introductory note to Sponsor's factual check on the External Assessment Centre report

Title: Parafricta Bootees and Undergarments to reduce skin breakdown in people with frail skin or at risk of pressure ulcers

Parafricta thanks the EAC for its assessment report, which we have read with interest and carefully reviewed.

Whilst we are in agreement with much of the EAC report, we have found four important factual inaccuracies (A-D) that may impact on the conclusions drawn. In addition, there are two comments (E-F) that we wish to draw to you attention.

In addition to our summaries in this cover note all factual inaccuracies are detailed in the tabular-format response as requested.

A. Interpretation of Lahmann papers.

The data presented by the two papers from Lahmann et al have been misinterpreted. As a result the conclusions drawn on pages 9, 30 and 61, based on the two papers Lahmann (2011a and 2011b) are incorrect. Consequently the report text contradicts Lahmann et al.'s validated conclusions that friction and shear are major contributing factors in the development of Grade I and II Pressure Ulcers and that pressure the major contributing factor for Grade III & IV.

We acknowledge that the information in this paper is not presented in the most transparent manner and have attempted to clarify below.

a. Lahmann (2011a) shows in a sample of 28,299 hospital patients that those with friction and shear problems have 5 to 6 times the average prevalence of category II Pressure Ulcers (PUs).
    i. The authors quote "According to Table 2 the highest PU prevalence rate of 18.4% was found in patients with problems regarding the item "Friction & Shear" and who had very or completely limited sensory perception. The column "percent of average" indicate that the prevalence in this group was more than 6 times higher (638.9%) than average. The size of this group was *n* = 977 patients, which was 3.5% of all patients."
    ii. The prevalence of any form of skin damage or decubitus ulcer in a patient population is always low and in this case the prevalence of skin problems caused by friction and shear was 7.5% with a further 17.3% identified at potential risk from friction and shear problems.

b. Lahmann (2011b) shows in a sample of 17,966 long-term care (LTC) residents that those with friction and shear problems have up to 4 times the average prevalence of PUs. In the LTC study the factors friction and shear are higher contributors to PU prevalence than moisture, mobility, activity, nutrition & sensory perception.
    i. They state "Tree analysis in Fig. 1 shows on the first level, that the strongest predictor for pressure ulcer grade 1–4 was 'friction and shear'

ii. They conclude "The prevalence in this group was 3–4 times higher than average.

13.9% was the percentage of patients in the whole population identified has having skin damage caused by friction and shear, with a further 8.2% identified as having the potential for this problem. (not atypical of the prevalence of decubitus ulcers in a patient population).

Thus we respectfully suggest that the text in §2.1 page 9, §3.11 page 30 and §6 page 61 should be amended to state that Lahmann 2011a and 2011b confirm the importance of friction and shear in PU prevalence.

B. Comparability of Cohorts in Smith et al

Table 6 showing the Waterlow Scores from the published study by Smith et al, on page 29, was supplemented by data in Appendix 5. The sponsors recognised that the published data in Table 6 was incorrect and the correct information was presented in Appendix 5. Using this erroneous information has led the EAC to suggest that the cohort not given Parafricta were more at risk of pressure ulcers than those given Parafricta when in fact there is demonstrated to be no statistical difference between the cohorts. The p-value shows the cohort without Parafricta was no more at risk of pressure ulceration than the cohort given Parafricta garments (and therefore the differences could be attributed to the addition of Parafricta).

Therefore statements in §1.3 page 6, §2.3.1 page 11, Table 1 page 18, §3.6 page 24, below Table 6 page 29, §3.11 page 30, §4.4 page 34 and §6 page 61 should be amended to make clear that the Waterlow score profiles of the two cohorts were statistically identical.

C. Length of stay and economic implications

The EAC's critique of the Length of Stay data in the Smith et al 2010 study (§1.2 page 5, §1.3 page 6, Table 1 Comment page 18, §3.6 page 24 and Table 7 Comment page 33) needs to be clarified regarding the two cohorts. The statement is made "There were no statistically significant differences in length of stay between cohorts 1 and 2, but the lengths of stay were not given." However, the data on length of stay is given in the EAC Report in §4.7.5.1 Table 8 page 40. Hence the Smith et al statement should be re-visited using the raw data.

This table demonstrates that there is no significant difference between the length of stay in **comparable pathways** irrespective of Cohorts.

However, it demonstrates that if patients do develop a pressure ulcer the length of stay is approximately doubled (21 & 17 days) when compared to those that did not develop a pressure ulcer (10 & 11 days) . There are of course significant costs associated with the consequent extra length of stay.

- **With respect to the per diem cost of those extra days stay referred to in the EAC document.**

Quality, Innovation, Productivity, Prevention challenge (QIPP) provides a User Guide advising on relevant costs to use when quantifying benefit from bed-day saved re:

https://www.evidence.nhs.uk/qipp. Page 18 advises users seeking to quantify reductions in the length of stay: *'Based on the assumption that utilisation of costs is greater at the start of an admission then using RC [Reference costs] for excess bed days may be the most appropriate type of cost to use.'*

- **Value of bed-days saved**
    - The sponsor notes the EAC preference is to use an excess cost per bed-day of £234 being the excess bed-day for skin disorders in the specialities of General Medicine and Trauma and Orthopaedics. These are taken from National Reference Costs 2012/13. The rationale for using these two wards seems to be because these wards were the settings for the clinical trial. However pressure ulcers can occur across the hospital. Across all specialties the excess cost of a bed-day is £255. Nevertheless there are significant savings using either figure.
    - The resource used to manage patients who are unable to reposition independently and have a pressure ulcer, or those who develop a pressure ulcer or go on to develop an infected pressure ulcer is considerably higher than that for a patient who has recovered from a disorder and waiting to be discharged. For the last the excess cost per bed-day may be the best valuation approach but it is a highly questionable assumption for those with pressure ulcers.

D. Hampton et al study

The EAC report's discussion and conclusions in §1.2 page 4, §1.2 page 5, §3.4 page 16, Table 1 page 18 and §3.6 page 24 relating to the ultrasound analysis extracted from the study by Hampton et al (2009) are incomplete and the function and diagnosis provided by the high-frequency ultrasound (HFU) is misinterpreted.

a. In the case of wound assessment, a normal area was compared to an affected area. HFU is an effective tool for the investigation of skin and soft tissue changes consistent with the documented pathogenesis of pressure ulcers (Quintavalle *et al*, 2006) and is capable of providing scientific, measurable and reliable outcome results.
b. In this study the HFU **scans** (not graphs) show the reduction of measured oedema in the sub-cutaneous tissue; they are not used to measure skin thickness in this application. Such scans are routinely used by clinicians to assess the presence of oedema and, hence, the level of tissue damage in patients.
c. The images used for diagnosis by the expert clinician using the technique would have been viewed in colour and conclusions made on that basis only.
d. The graphs, in Figures 4, 5 and 11 of the paper, show the summation of the patient data for each of the groups as indicated by the graph title, e.g. heel treated with Parafricta or Control [non Parafricta] heel. In each case the profile of a normal heel is also shown. The healthy normal HFU profile is used as an important additional 'control' for both the heel and the sacral data but this is not explicitly mentioned in the EAC report.
e. All patients are measured at 0, 2, and 4 weeks, so the data set is complete.
f. In the critique of the statistical analysis on page 24, the statement "It is unclear whether the graphs are depicting skin oedema and its resolution or not. The results in **Error! Reference source not found.** are difficult to interpret as it is unclear what 'Diff' refers to (oedema, skin thickness or pixel number)" is made.

For clarification, the graphs show skin oedema and compare it with a normal curve. The graphs demonstrate that after intervention the scans of sub-epidermal and dermal oedema move towards the normal curve thus showing that tissue damage is reversed in the active heel when compared to the control heel and in the sacrum when compared to a normal graph.

Figures 7, 8 & 9 in the provided documents *NHSIL Health Economics Unit paper copy for Drug Tariff Jan 31 2010 pdf* and *Parafricta Trial Final Results JCN Statistical Analysis* gives the statistical analysis methodology and results for the Hampton et al (2009) data. The difference in pixel number per time stage reflects resolution of oedema. The conclusions are that the application of the Kolmogorov-Smirnov statistical test showed that the symptoms of the treated heel had improved significantly over time when compared to the control heel at times 0 and 4 weeks and the level of oedema as measured by ultrasound mean pixel distribution had moved significantly towards the profile of normal heels.
The inclusion of these Figures 7-9 would help clarify this conclusion.

Comments:

E. Economic Model

We would welcome greater transparency of the economic model used by EAC.

For example, there is no goodness of fit data provided for the regression and it is unclear why the median is 2 times the mean value for the length of stay when in most cases the mean is usually greater than the median. We were surprised in the large difference between the raw values and predicted values in Table 20.

There is a degree of confusion between the measures used for the projected economic benefit in community and hospital settings. To clarify:

- In the Hospital model, the savings are per at-risk patient episode
- In the community model, savings are per year per at-risk patient .

Confusion between these measures has led to the statement concerning the Sponsor's cost model at the end of §1.4 on page 7: "Also that the pressure ulcer was there for a whole year", which is incorrect and should be deleted.

F. Section 2.3.3: Comparators

Pressure Redistributing/Reducing Surfaces (PRS) are, almost without exception, employed in at risk patients in the hospital or community. NICE added Sheepskins and Pressure Reducing Bootees as comparators, however the Sponsor would like to point out that both are:

a. Specifically targeted to reduce or redistribute pressure whilst Parafricta is prescribed to reduce friction and shear, the other two extrinsic factors causing skin and tissue breakdown in PUs. Therefore they are not direct comparators.
b. The use of these two comparators is intermittent compared to more widespread use of PRS.