[redacted]
National Institute for Health and Clinical Excellence
Level 1A City Tower
Piccadilly Plaza
Manchester
M1 4BD

24 August 2011

Response to DSU queries regarding model structure and additional analyses in PAS cost-effectiveness analyses

Dear [redacted],

Thank you for your call earlier today. We understand that the Decision Support Unit (DSU) has asked for clarification on an issue related to our revised economic model operation within Excel. DSU has also asked for two additional cost-effectiveness assessments to be carried out to assist decision-making at the next Appraisal Committee meeting around the proposed patient access scheme (PAS).

Our responses to the queries are found below. [redacted]. Should you have any further queries, please do not hesitate to contact me.

Kind Regards,

[redacted]

Roche Products Limited
6 Falcon Way
Shire Park
Welwyn Garden City
Herts, AL7 1TW
Registered in England 100674
[redacted]
Tel. [redacted]
Fax [redacted]
Email: [redacted]

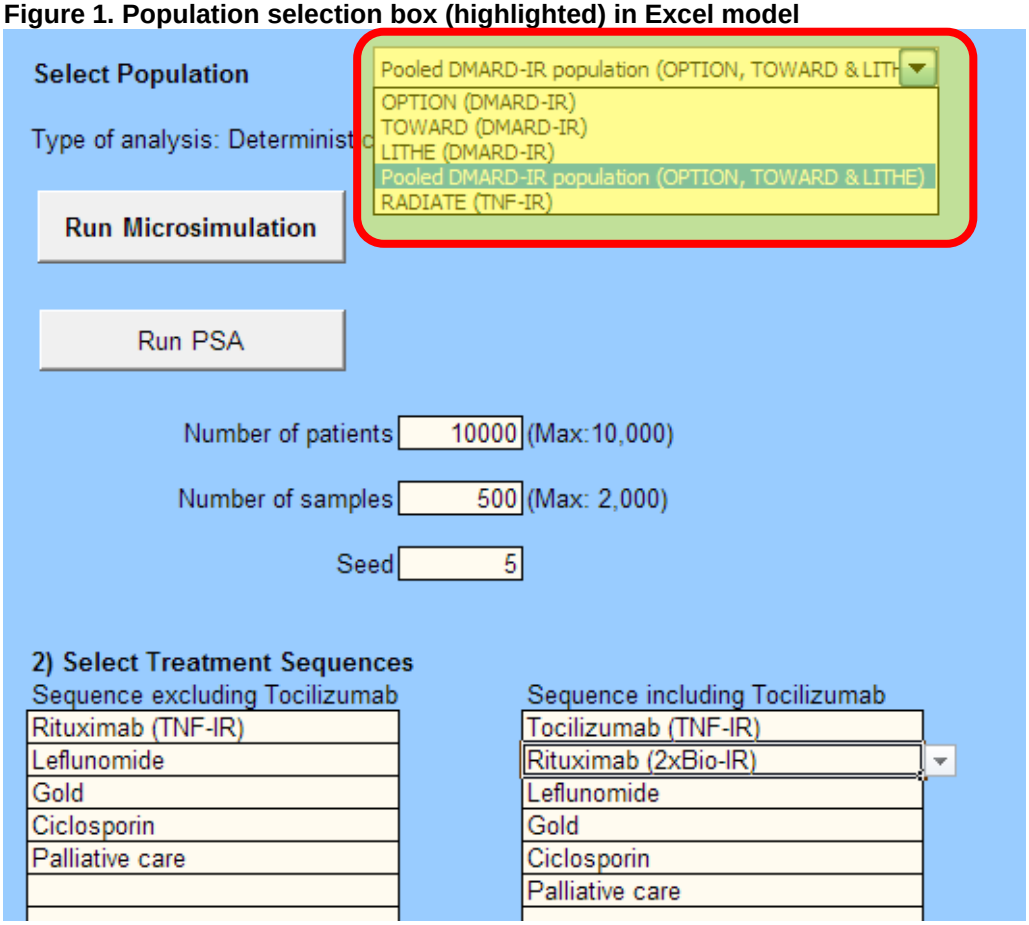
Notes about model design and population selection

The DSU has queried how the Excel model should be set up to run analyses in the DMARD-IR and TNF-IR populations.

Specifically the DSU's query relates to a drop-down box in the Excel model labelled 'Select Population', which was previously used to specify the trial populations from which efficacy data were were drawn. An illustration of the drop-down box is shown below in
Figure 1.

Selections within this box limited analysis to either anti-TNF drug inadequate responder (TNF-IR) or disease-modifying anti-rheumatic drug inadequate responders (DMARD-IR).

Figure 1. Population selection box (highlighted) in Excel model



The DSU has queried whether this drop-down needs to be set to reflect the population of interest when modeling treatment sequences involving the DMARD-IR or TNF-IR populations (for example, tocilizumab → rituximab → supportive care in the TNF-IR population).
The answer is no.

This drop-down is obsolete in the latest model version and should have been removed. In the place of the 'population' drop-down functionality, the treatment sequence drop-down boxes now contain 'TNF-IR' or '2xBio-IR' versions for relevant drugs, which should be selected to appropriately reflect the population and sequence of interest. As an example, the Excel model in Figure 1 has been set up to model costs and QALYs of tocilizumab followed by

rituximab compared to rituximab alone in the TNF-IR population.

We can hereby confirm that **the analyses presented thus far in our PAS submission use this functionality and are correct.**

Additional analyses requested

To inform Appraisal Committee decision-making in the context of the prior TA198 appraisal, additional analyses are required. DSU has requested that costs and QALYs (with and without PAS) for an additional two treatment sequences be calculated and appropriately compared to standard care as follows:

1. TR versus ER in the DMARD-IR population
2. TR versus R in the TNF-IR population

Note: T = tocilizumab, R = rituximab, E = etanercept

We present these results as pairwise comparisons in Table 1 and
Table 2 respectively.

Table 1. Cost-effectiveness results - TR versus ER (DMARD-IR population)

	ER	TR	TR with PAS
Total costs (£)	88,244	79,453	[redacted]
Difference in total costs (£)		-8,790	[redacted]
LYG	26.00	25.81	25.81
LYG difference		-0.073	-0.073
QALYs	8.466	8.085	8.085
QALY difference		-0.381	-0.381
ICER (£/QALY)		23,047†	39,595

Abbreviations used in treatment sequences: E: etanercept; R: rituximab; T: tocilizumab. Please note that ICERs in table take into account decimal places not shown, hence there will be a small discrepancy between figures presented here and any calculated by hand from this table.

Please note in Table 1 that the TR treatment sequence is associated with less benefit and lower costs than ER, hence ICERs should be interpreted with caution.

Table 2. Cost-effectiveness results - TR versus R (TNF-IR population)

	R	TR	TR with PAS
Total costs (£)	53,608	74,551	[redacted]
Difference in total costs (£)		20,943	[redacted]
LYG	25.37	25.71	25.71
LYG difference		0.135	0.135
QALYs	7.134	7.819	7.819
QALY difference		0.685	0.685
ICER (£/QALY)		30,574	22,690

Please note that ICERs in table take into account decimal places not shown, hence there will be a small discrepancy between figures presented here and any calculated by hand from this table.

The addition of one extra treatment sequence (TR) in the DMARD-IR population necessitates an update to the incremental analysis we supplied for the DMARD-IR population previously.

This updated incremental analysis can be found in Table 3. In this analysis, the TR sequence has been included, ranked as producing the fewest QALYs in the DMARD-IR setting. By comparison, the ER option is associated with QALY gains but also greater costs. The ICER comparing TR to ER suggests that ER does not represent a cost-effective improvement in QALY gains compared to TR.

Compared to the TR option, subsequent treatment sequences involving tocilizumab (TER, ETR, ERT) all represent cost-effective incremental improvements in QALYs. This finding is similar to that presented in our previous version of the incremental analysis, in which TER, ETR and ERT were all cost-effective compared to ER.

Table 3. Base case incremental results (DMARD-IR population) with PAS

Treatment sequences	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
TR (with PAS)	[redacted]	8.085	-	-		
ER	88,244	8.466	[redacted]	0.381	[redacted]	[redacted]
TER (with PAS)	[redacted]	8.618	[redacted]	0.152	29,932	5,716
ETR (with PAS)	[redacted]	8.984	[redacted]	0.366	30,251	30,716
ERT (with PAS)	[redacted]	9.066	[redacted]	0.082	28,403	8,134

Please note that ICERs in table take into account decimal places not shown, hence there will be a small discrepancy between figures presented here and any calculated by hand from this table.

From what we understand, the TNF-IR population comparison will not require additional incremental analyses.

END