CONCLUSION
3.1 OCRS-BID bioequivalent to Cefclor CD 500mg

6.1.1 A patentable twice-a-day formulation has been developed using xanthan gum and sodium alginate as rate controlling polymers. The product has been stabilized using calcium sulphate and hydroxypropyl methylcellulose phthalate. The prototype formula is shown in Table 3.21 and the process thereunder.

6.1.2 The proposed specifications for the product and the standard testing procedure is enclosed as Annexure 14.

6.1.3 Based on the satisfactory data, after 3 months at the accelerated storage condition, a 24 month shelf life can be assigned to the product in Aluminum strip pack (Annexure 3).

6.1.4 The product is bioequivalent with Cefclor CD of Eli Lilly, USA in fed and fasted conditions in terms of C\text{max} and AUC (Tables 5.4 & 5.5).

6.2 OCRS-intervention of conventional 500mg TID cefaclor for a bioavailable and stable, 1.0g, once-a-day preparation with probenecid

A bioavailable once-a-day intervention was achieved by decreasing the dose of the drug substance from 1.5g to 1.0g by co-administering with 1g of probenecid. A 10-hour profile \textit{in-vitro}, showed desirable T>MIC, C\text{max} and AUC \textit{in-vivo}.
6.3 OCRS intervention of conventional 500mg TID cefaclor for a 
bioavailable and stable, 1.5g, once-a-day preparation

6.3.1 A patentable OD formulation of Cefaclor has been developed using 
xanthan gum and sodium alginate as rate-controlling polymers. The product 
has been stabilized using calcium sulphate and hydroxypropyl 
methylcellulose phthalate. The prototype formula is shown in Table 4.14.

6.3.2 The proposed specifications for the product and the standard testing 
procedure are enclosed as Annexure 15.

6.3.3 Based on the satisfactory data, after 3 months at the accelerated storage 
condition, a 24 month shelf life can be assigned to the product in 
Aluminum strip pack (Annexure 11).

6.3.4 Following a number of bioavailability studies, we were able to establish an 
OD intervention of an existing TID/BID preparation with a desired in-vitro 
and in-vivo profile. It was established that a 10 hour release profile, offered 
an optimal extension matching the absorption window thereby maximizing 
T>MIC (1µg/mL) and resulting in T/R of AUC and Cmax between 80- 
120% of that obtained on administering 500mg conventional capsules three 
times a day in fed healthy human volunteers. The t1/2 of the OD product was 
extended beyond that of the conventional product. (Table5.6). This satisfies 
the four main criteria for an OD formulation.

6.3.5 The OD matrix systems developed show a zero-order release profile and 
exhibit anomalous behavior.

6.3.6 A perfect (r²=0.99) correlation has been established between amount of 
drug released in-vitro and drug plasma concentration in-vivo.

6.3.7 In view of the large number of variables like pH-dependent solubility, 
permeability, absorption window, t1/2 etc while designing a controlled 
release system, the strategy and value of zero-order release and/or in-vitro 
in-vivo correlation is yet to be established. Large number of such studies, 
need to be conducted, using drug substances with aforementioned variables 
to draw a meaningful conclusion.