Recommendations of the SEC (Cardiovascular & Renal) made in its 118th meeting held on 27.01.2023 at CDSCO (HQ), New Delhi:

S.No.	File Name & Drug Name, Strength	Firm Name	Recommendations
SND Division			
1.	SND/MA/22/000295 Icosapent Ethyl Capsules 599mg/1000mg	M/s. BDR Pharmaceuticals	The firm presented its proposal of manufacture and marketing of Icosapent Ethyl Capsules 500mg and 1000mg for the indication "used as an adjunct therapy for severe hypertriglyceridemia (TG levels > 500mg/dl and to reduce the risk of cardiovascular event in certain patients with elevated triglycerides)" along with BE and CT waiver justification before the committee. The committee noted that the drug product is already approved by USFDA and also available for clinical use in USA. After detailed deliberation, the committee recommended for grant of permission for manufacture and market of the applied drug product for the proposed indication subject to condition that the firm should submit PMS data to CDSCO after marketing of the drug product in Indian market.
2.	SND/MA/22/000268 Icosapent Ethyl capsules 1gm	M/s. Dr. Reddy's Laboratories	In light of earlier SEC recommendation dated 08.12.2022 & 09.12.2022 the firm presented their proposal alongwith some efficacy data of their product marketed in USA and in-vitro data/comparative data which have been submitted during approval of their product in USA before the committee. The committee noted that the drug product is already approved by USFDA and also available for clinical use in USA. After detailed deliberation, the committee recommended for grant of permission for manufacture and market of the applied drug product for the proposed indication subject to condition that the firm should submit PMS data to CDSCO after marketing of the drug product in Indian market.

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3.	SND/MA/21/000482 Ticagrelor SR Tablets 120/180mg	M/s. Theon Pharmaceuticals	In light of earlier SEC (Cardiovascular and renal) recommendation on its meeting held on 11.10.2022 the firm presented the raw data for BE studies of Ticagrelor SR Tablets 180mg/120mg before the committee along with the justification for the following queries raised by the committee in meeting i.e 1. Values of Cmax for Ticagrelor and its metabolite in test product is significantly higher than that of reference product in both the BE studies. 2. There are higher percentages of adverse events i.e drop in haemoglobin values in subjects. 3. There are significant number i.e (around 20%) lost to follow up subjects in BE study of Ticagrelor SR Tablets 120mg. After detailed deliberation, the committee opined that the firm has not submitted satisfactory reply for the above mentioned queries and also noted that firm has not conducted the causality analysis for higher percentages of adverse events i.e drop in hemoglobin values in subjects. Committee also noted that recently the Innovator of the Ticagrelor tablets M/s Astrazeneca has raised its objection on feasibility of sustained release formulation of Ticagralor and raised the issue before the committee on its 115th SEC (Cardiovascular & Renal) dated 08.12.2022 that the regional absorption study by Tengli R and Maya J et al clearly demonstrates both AUC and Cmax for Ticagrelor declines significantly further down in the GI tract. These facts combined with Astrazeneca's significant efforts to develop a sustained release formulation without succeeding demonstrate that Ticagrelor has properties that do not support development of a once daily sustained release formulation with same efficacy and safety as the immediate release formulation with twice daily dosing. None of the formulations gave the desired controlled-release PK profile which was

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			to achieve a mean percentage inhibition response of at least 50% inhibition of final extent at 24 hours post-dose. The retention time in the stomach can be slightly increased with food. However, the relatively small increase in retention will vary with type of food, amount of calories and other factors. It is important to understand that the lack of successful PK/PD data is not matter off a "poor" formulation design but an inherent property of the API. In keeping view of the above, the committee after detailed deliberation did not recommend for grant of permission for clinical trial to M/s. Theon Pharmaceuticals. The committee also recommended that the clinical trials and BE study permissions granted to various firms so far by CDSCO should be kept on hold and all such studies shall be discontinued till the matter is reviewed further.
4.	SND/MA/20/000194 Ticagrelor SR Tablets 120/180mg	M/s. Exemed Pharmaceuticals	The firm did not turn up for presentation.
5.	SND/MA/20/000265 Ticagrelor SR Tablets 120/180mg	M/s Mascot Health	During deliberation of similar proposal made by M/s. Theon Pharmaceuticals the committee noted that there are higher percentages of adverse events i.e drop in haemoglobin values in subjects. Committee also noted recently the Innovator of the Ticagrelor tablets M/s Astrazeneca has raised its objection on feasibility of Sustained Release formulation of Ticagralor and raised the issue before the committee on its 115th SEC (Cardiovascular & Renal) dated 08.12.2022 that the regional absorption study by Tengli R and Maya J et al clearly demonstrates both AUC and Cmax for Ticagrelor declines significantly further down in the GI tract. These facts combined with Astrazeneca's significant efforts to develop a sustained

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			release formulation without succeeding demonstrate that Ticagrelor has properties that do not support development of a once daily sustained release formulation with same efficacy and safety as the immediate release formulation with twice daily dosing. None of the formulations gave the desired controlled-release PK profile which was to achieve a mean percentage inhibition response of at least 50% inhibition of final extent at 24 hours post-dose. The retention time in the stomach can be slightly increased with food. However, the relatively small increase in retention will vary with type of food, amount of calories and other factors. It is important to understand that the lack of successful PK/PD data is not matter off a "poor" formulation design but an inherent property of the API. In keeping view above committee after detailed deliberation did not recommended for grant of permission for clinical trial to M/s. Theon Pharmaceuticals. The committee also recommended that the clinical trials and BE study permissions granted to various other firms so far by CDSCO should be kept on hold and all such studies shall be discontinued till the matter is reviewed further.
FDC Division			
6.	FDC/MA/22/000259 Cilnidipine IP 20mg + Metoprolol Succinate IP 47.50mg eq. to Metoprolol Tartrate (As ER) 50mg Tablets	M/s. Ajanta Pharma Ltd.	The firm did not turn up for presentation.
7.	FDC/MA/22/000293 Sacubitril Sodium eq. to Sacubitril + Valsartan IP	M/s. Intas Pharmaceuticals Ltd.	The firm presented its proposal alongwith BE Study protocol as well as justification for developing FDC formulation of Sacubitril and Valsartan tablets with individual API as Sacubitril Sodium & Valsartan.

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	(97mg + 103mg) film coated tablet		After detailed deliberation, the committee recommended that firm should submit the published literature, articles in peer reviewed journal, etc in this regard for further review by committee.
8.	FDC/MA/22/000241 Chlorthalidone IP 6.25mg/12.5mg + Cilnidipine 5mg/10mg + Bisoprolol Fumarate 5mg/10mg tablets	M/s. Windlas Biotech Ltd.	In light of the earlier SEC recommendation dated 08.12.2022 & 09.12.2022, firm presented the revised CT protocol. After detailed deliberation, the committee recommended for grant of permission for conducting the Phase III Clinical Trial.
9.	FDC/MA/22/000344 Dapagliflozin Propanediol Monohydrate eq.to Dapagliflozin 5mg + Sacubitril/Valsartan as sodium 50mg/100mg/200mg tablets	M/s. Ravenbhel Healthcare Pvt. Ltd	In light of earlier SEC recommendation dated 08.12.2022 & 09.12.2022, firm presented its proposal. Committee noted that Dapagliflozin, because of its PK and Pharmacological diuretic effects, cannot be prepared as FDC with Sacubitril, Valsartan for twice daily administration as proposed by the firm. After detailed deliberation, the committee reiterated its earlier recommendation.