BACKGROUND AND OBJECTIVES
ED (Early Dialogue) processes between manufacturers, Regulators and HTAs were developed to improve quality of evidence and patient access to new medicines. In four different occasions, three of which were within SEED as the pilot project financed by EC involving 14 HTA bodies, Sanofi engaged in HTA ED with or without Regulators. Here, we make an account of lessons learnt and suggestions for future improvements.

RESULTS AND DISCUSSION
The four early dialogues were conducted at different phases of the R&D process: Chronic disease 1 ED was based on Phase Ila results, Chronic disease 2 on Phase Ib, Cancer and Rare diseases both on Phase I. HTA bodies attendance was satisfactory; EMA was involved as observer three times and as active participant during one occasion. Patients and experts were not always involved (see Figure 1 for meeting attendees). The areas in which Sanofi was seeking advice are described in Table 1.

PREPARATION AND PARTICIPATION:
The time spent to prepare was different across the teams, reaching up to a maximum of 8 months effort for 18 people from different company functions, including Regulatory, HEOR, Biostatisticians, Market Access, Clinical Team, Medical Affairs, Medical Writing. Teams involved in the whole process, from request of submission to advice, were completely or mostly satisfied with the briefing book template and the clarification points. When EMA was actively involved, their clarification points were particularly well formulated, adding value to the meeting. Only in the first 2013 experience, was the preparation phase more difficult given a template was not yet available.

CONSULTATION:
Generally speaking the level of discussions was high and productive. Three improvement areas have been mentioned as described in Table 2. 1) flexibility around topics to be raised during the meeting; 2) consensus and conclusive advice; 3) comprehensive and univocal final report. Other minor comments were also made to improve other aspects. In one situation there was a mismatch in the expertise involved by EMA vs by the company (e.g. a biochemist) and no debate was possible to that respect. Therefore, a better coordination about competencies to be involved in the meeting was recommended to make sure an expert interlocutor is present to allow technical discussion.

OUTPUT:
Sanofi team was largely satisfied about usefulness of advice received and ability to incorporate it into the evidence generation plan. When consensus was reached, clear and univocal advice was given on outcomes, comparators, population and trial design, indirect comparison, F&E, patient stratification, elements to be factored in the economic model, according to the issues under discussion.

In all cases, the advice has been to some extent followed and items have been modified accordingly in the evidence generation plan; similarly, Market Authorization Application filing strategy has been fine-tuned in some cases. As to the overall process and its governance, improvement was seen over time and satisfaction has increased with this regard.

CONCLUSIONS
Sanofi level of satisfaction of the ED experience was generally high, allowing to pressure test evidence development plans and scenarios, while garnering feedback on critical items from multiple countries. Some areas of improvement have been identified. Despite the fact that the SEED pilot objective was not to reach a consensus, it would be desirable in the future to reach an alignment on final recommendations. This would increase the probability that a company’s evidence generation plan is going to meet the different HTA bodies and, when relevant, regulatory requirements. As a consequence, ED overall impact would increase, although the implementation of the recommendations remains responsibility of the company, also taking into account business decisions and requirements in other regions.

Finally, assessment of ED evolution needs to be integrated in the context of a changing environment and particularly in the debate around systematic approach to joint relative efficacy and effectiveness to be conducted at EU level as a first step in the process of Health Technology Assessment at level of the member states. If and how these two game changers will be interconnected will determine the future value evidence generation strategies. Hopefully the SEED experience will inform decision making and road map definition in this transformative and new pathway.