1. **Alignment of the current guidance development processes**

***General comments on theme***

* **Would you like to provide general comments in relation to the proposals in this theme?**

(Options: Yes, I would like to provide general comments on this; No, I do not have general comments on this)

No

* **If yes: Please share your general comments here:**

(Open text box, 9,999 character limit)

***Comments on specific proposals***

* **Would you like to add comments relating to specific proposals? If so, please select all that apply from the list below:** (see appendix 1 for full list of proposals, including paragraph references)

Para 37: FPM supports the principle of alignment of all phases of the health technology guidance development process. As an objective we believe that this is a sensible approach, providing that there is alignment around a single, simple process.

The FPM membership includes people responsible for the research and development of medical devices and diagnostics, as well as pharmaceuticals and biopharmaceuticals. We therefore would like to note that the devices and diagnostics industry is small and has very limited resources. We recommend that NICE offers additional and bespoke help and guidance throughout the process to those working in these fields.

We agree with provision of information to enable transparency. However, in doing so, there is risk of providing an overview of the science and the assessment of evidence from the company perspective. We would encourage the development of the layperson summary of evidence to be jointly developed or independently developed by medical writers and reviewed by NICE committee and company.

We would recommend harmonisation in use and meaning of terms across NICE sectors and divisions.

Para 59: We agree with the general principle of a 'Summary of Information for Patients' (SIP). However, we would recommend that NICE consider how pharmaceutical companies could appropriately provide a SIP with their evidence submission and work with companies to ensure that guidance is compatible with ABPI Code of Practice restrictions. We would also recommend that companies ensure that the patients and carers can input to the SIP to reflect on whether it measures what is important to them. It should also be ensured this activity is also aligned with the ABPI Code of Practice.

Para 71: It appears that "diagnostics guidance and medical technologies" are not connected to the medical condition for which they have been developed. As an example, any genetic test on monogenetic diseases should be evaluated according to its specific merits. There seems to be an unwelcome opportunity for subjective and arbitrary judgement on these topics, apparently with the potential loss of opportunity for stakeholders to comment on content of the final guidance. We would recommend that NICE reconsider this proposal.

Para 78: FPM would seek clarity on the specifics of the ‘multiple technology assessment for Highly Specialised Technologies’ mentioned.

* **If specific proposals selected: How strongly do you agree or disagree that you support the proposals related to:** (all selected proposals will be listed individually here. Options: Strongly agree, agree, neither agree nor disagree, disagree, strongly disagree, don’t know/ NA.)

Note: we are trialling the inclusion of this question to help inform our interpretation and analysis of feedback and identify any issues more effectively, we do not propose to publish your responses.

* **If specific proposals selected: Please use this space to share any comments on the proposals:** (all selected proposals will be listed here. Open text box, 9,999 character limit)

***Final comments on theme***

* **Please share any final comments on the proposals in this theme below, including any areas that have not been covered or other proposals which you think should be considered.**

(open text box, 9,999 character limit, you can also upload supporting documents relating to this here.)

1. **Opportunities for new process improvements and ways of working**

***General comments on theme***

* **Would you like to provide general comments in relation to the proposals in this theme?**

(Options: Yes, I would like to provide general comments on this; No, I do not have general comments on this)

Yes

* **If yes: Please share your general comments here:**

(Open text box, 9,999 character limit)

FPM considers this section to be somewhat generic and not specific enough on the desired objectives and targets for improvement. Clearly specifying goals for e.g. appraisal processes, reductions in access inequality and other stated objectives would be recommended.

Real World Evidence / Data is viewed as instrumental for many technology appraisals and, perhaps more than already happens for products, post-access new data should be reviewed on a frequent basis (in addition to PMRs) and potentially enable price adaptations, if warranted, in view of decreasing uncertainties and greater confidence in the value delivered by the new medicine. This would especially be relevant to ensure access to orphan drugs and/or HSTs. Early discussion with patient organizations could enable insights on collection of robust RWD/RWE, that could help inform NICE decision making.

Value (both costs and benefits) should be appraised from the societal perspective and not solely from the healthcare budget impact/point of view. This should be the standard anyway but is especially pertinent for certain new, possibly one-off treatments with a very high acquisition cost but potentially life-long benefits (including savings on alternative lifelong treatments).

It is important to recognise that biosimilars are not equivalent to generic small molecules and must be assessed on the clinical evidence and not the price difference from the originator, by automatically assuming the exact same profiles. Switching a patient’s treatment to a biosimilar based on cost is not always preferable. There may be individual tolerability and/or efficacy issues, which could cause the patient physical and/or mental distress. If only the ‘cheapest’ product is endorsed by NICE and paid for by the NHS, physicians are curtailed of relevant therapeutic choices and patient care can be affected. Additionally, if we consider pharmacoeconomic implications of product replacements inducing serious side-effects, subsequent treatment costs may easily outweigh prescription savings whilst coping with such complications. We would encourage NICE to strive for meaningful therapeutic choices.

With regards to reducing health inequalities – we would seek clarification on whether it is being proposed that there is an economic argument for differential use or adoption based on regional or other differential need, based on the magnitude of impact or cost benefit in deprived vs less deprived areas? This may be a helpful subpopulation analysis and a way of piloting use in the areas of highest need and thus value. If this intends to end the postcode lottery effect of (non)adoption of new technologies across the UK, that seems a laudable improvement, as long as it doesn't have the effect of leading to new inequalities in the reverse direction.

Digital health technologies do indeed represent a major change in healthcare provision as demonstrated by, for example, US regulatory approvals for mobile phone “Apps” as therapeutics.

Clarity over the qualification of an “Expert” would be helpful. We agree it is important to maintain/increase clinical and technical/scientific expertise relating to the technologies and their implementation available to NICE when assessing these technologies. The term “clinical area” in this respect is somewhat unclear. The recognition that assessment of diagnostics requires an expertise beyond that available to patients and clinical experts is appreciated and supported. However, it is suggested that this may also be the case for other “high tech” innovations in Medical Technologies and Highly Specialised Technologies.

Transparency about whether or not a company had sought NICE scientific guidance presumes that this guidance is of itself, of value. Evidence for this presumption would be helpful. Paragraph 130 suggests that the appraising committee must not be informed that scientific advice had been sought in order to avoid bias in the appraisal. This could seem to suggest that a company which seeks scientific advice and delivers the required data by conducting agreed studies might still find its submissions compromised? We seek clarity on this point.

The proposals for a parallel track and timeline for regulatory approval and NICE guidance is strongly supported but presupposes that the company submitting their technology for appraisal has the resources to run this parallel track. It will be important to avoid duplicating requests for information or offering contradictory proposals or recommendations. We seek clarity on how this will operate.

With respect to the technical engagement process, we would recommend that NICE develop further guidance on: Clarifying misunderstanding of the evidence; Clarifying clear areas of clinical and economic uncertainty in the evidence; and agree on possible means of bridging uncertainty incorporating managed access into these discussions and possibilities of novel analyses or data collection.

***Comments on specific proposals***

* **Would you like to add comments relating to specific proposals? If so, please select all that apply from the list below:** (see appendix 1 for full list of proposals, including paragraph references)

Para 85: We welcome greater foresight into selection of experts, disclosure of experts and whether they represent their individual opinions &/or that of the body they represent. All relevant TA experts should be at committee meetings to address clinical uncertainties to be quorate. This is particularly important where a single technology impacts on different organ systems (e.g. cardiologist, nephrologist, endocrinologists). We recommend that patient evidence should form a routine part of information presented to the committee. What will be the objective criteria for the determination to seek or not seek patient evidence?

Para 95: We would recommend that NICE provide recommended timelines for company submission to NICE in parallel with EMA processes. To ensure efficiency in the clinical submission, NICE should be accepting of data submitted for marketing authorisation (e.g. module 2 summaries) unless new evidence emerges in the interim which could be provided in additional addendums.

The scale of individual drug-indication pairings or medical technologies that are in the development pipeline for regulatory approval over the coming years could rapidly absorb a significant proportion of capacity within the NICE evaluation work programmes. This is a crucial point: the line extension business in medicines is obvious as more and more molecular mechanisms are targeted which may be involved in more than one pathology. This idea to evaluate the mechanism in the first indication and any other should be emphasized.

Para 110: We agree with this, if the process is agile and fast to determine / ensure that is in the same disease area and not just the same class and that a comparative assessment is preferred.

Para 114: For cancer medicines such as checkpoint inhibitors, could a mechanistic rather than a taxonomic assessment of the indication be considered?

Para 116: With the current QALY threshold still set at £30,000, if this is the entry hurdle based on an ICER, most therapeutics of rare diseases do not need evaluation as they are (often) much more expensive than chronic applications. We are concerned about the proposal to reject company submissions based on unfeasible ICER. Transparency and an explanation of the process of how this is considered and how this would impact rare diseases is required. We propose that the cost in a certain timeframe or a lifetime cost, so assess different value and accrual of benefits rather than a direct QALY approach. An approach might be, for example, to help define the clinical use of a product so that the medical value becomes more obvious. This suggestion would complement the subsequent bullet point about treatment eligibility criteria.

Para 123: If there is evidence and approval for all indications we agree with this proposal. If, however, there is not full approval of all indications (as clinical evidence is required for the MAA) then it should be limited to approved indications vs the originator rather than assumed to be equivalent in the absence of evidence.

Para 126: Depending on whether NICE already uses the societal perspective for both costs and (economic effects of) benefits, purely focussing on budget impact for the NHS may discard drugs that (also) have important benefits outside the pure efficacy/effectiveness / safety elements.

Para 130: This proposal seems potentially very counterproductive, as it raises the possibility that the Committee/teams may criticise/reject evidence that was collected as a result of prior scientific advice. The feasibility of not acknowledging that advice has been obtained and how it was implemented in the evidence base seems low, as acknowledging this seems a rather necessary element in the dossier writing.

Para 131: We generally agree with this proposal. However, if a company followed the advice and NICE's view changed then this should be made clear. NICE advice should be binding (data notwithstanding) in principle to be adhered to by all and to ensure that the decisions follow the principles behind the advice and the evaluation of the evidence within those parameters.

* **If specific proposals selected: How strongly do you agree or disagree that you support the proposals related to:** (all selected proposals will be listed individually here. Options: Strongly agree, agree, neither agree nor disagree, disagree, strongly disagree, don’t know/ NA.)

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* **If specific proposals selected: Please use this space to share any comments on the proposals:** (all selected proposals will be listed here. Open text box, 9,999 character limit)

***Final comments on theme***

* **Please share any final comments on the proposals in this theme below, including any areas that have not been covered or other proposals which you think should be considered.**

(open text box, 9,999 character limit, you can also upload supporting documents relating to this here.)

1. **Commercial and Managed Access processes**

***General comments on theme***

* **Would you like to provide general comments in relation to the proposals in this theme?**

(Options: Yes, I would like to provide general comments on this; No, I do not have general comments on this)

Yes

* **If yes: Please share your general comments here:**

(Open text box, 9,999 character limit)

The proposals in this section generally seem well thought through and are strongly supported, with the proviso that they must be simple and easy to implement. Specifically, Data Collection Agreements must be limited and respect the nature of devices and diagnostics.

It is notable that the ERG and BMJ response to company submission as well as summaries to various committee meetings (e.g. ACD) has overview of data gaps. There could be a clearer description incorporated into a summary table at the beginning.

We welcome the opportunity for process oversight of the DCA. More clarity in process is needed, including the types of DCA considered and assessment of acceptability. Also, more time may be needed as part of the overall process if NICE are consulting with academic groups to seek feasibility of such DCA.

We would encourage increasing the limit of company representatives from 2 to 3. Currently, it is usually a physician (usually medical affairs) and market access person at the meeting. The third company person would enable greater depth of discussion around scientific issues e.g. provision of health economic input or clinical development.

The proposals related to managed access and data collection should be enabled by digital data collection, real time assessment to modulate (maintain) value, and include real world data and outcomes. As this may involve valuable data generated in non-UK countries, NICE/MRHA/UK government should aim to facilitate alignment with data protection regulations in other countries especially EU.

***Comments on specific proposals***

* **Would you like to add comments relating to specific proposals? If so, please select all that apply from the list below:** (see appendix 1 for full list of proposals, including paragraph references)

No

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***Final comments on theme***

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1. **Highly Specialised Technologies - vision and principles**

***General comments on theme***

* **Would you like to provide general comments in relation to the proposals in this theme?**

(Options: Yes, I would like to provide general comments on this; No, I do not have general comments on this)

No

* **If yes: Please share your general comments here:**

(Open text box, 9,999 character limit)

***Comments on specific proposals***

* **Would you like to add comments relating to specific proposals? If so, please select all that apply from the list below:** (see appendix 1 for full list of proposals, including paragraph references)

Para 173: Could NICE clarify if there is a quantitative definition of "serious", “severe” and “ultra-rare”, which entitles each patient in those categories to benefit? Those diseases are mainly based on genetic defects. Does this vision outweigh mono-genetic diseases against multi-genetic or complex inborn diseases with no causal treatment options? The ‘Rare Disease Network’ refers to diseases with rather varying incidences (e.g. nephrotic syndrome vs Pompe's disease). How will NICE prioritise such diseases economically?

Para 174: HST should not only provide and emphasize access to treatment but also to clinically relevant diagnostics which, especially in the case of lifelong conditions, may allow detection of complications early, even before clinical onset. This could enhance the quality of treatment through early interventions. The consideration of both therapeutics and diagnostics should be part of any evaluation project.

Para 176: The landscape of rare disease technologies has evolved and changed since the HST programme’s inception. There has been an increase in the number of treatments in development across the spectrum of rare disease. We agree with the thrust of the proposal but seek clarification on whether prioritisation is part of the evaluation process or an in-house a priori decision, resulting in a top-down list?

Para 186, point c: This criterion excludes several disease conditions on the list of the Rare Disease Collaborative Network. Does the last sentence mean that a technology will be used specifically for one disease as long as the respective NICE guidance is in place?

Para 186, point e: It is appreciated that NICE clearly asks for innovations rather than indication-extensions. This may fuel access to innovative medicines, diagnostics and disease relevant services.

Para 186, point f: We agree with this principle and it should be viewed as a foot in the door to wider assessment, unless clearly different dose, presentation etc restricts use. It is, however, important to consider lifetime value and cost even if timescales are different. We would recommend that NICE clarifies these potential factors. The lifetime value and also the broader value (costs and benefits) to society, outside the "purely" medical efficacy/effectiveness/safety/QoL value, should be counted.

* **If specific proposals selected: How strongly do you agree or disagree that you support the proposals related to:** (all selected proposals will be listed individually here. Options: Strongly agree, agree, neither agree nor disagree, disagree, strongly disagree, don’t know/ NA.)

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***Final comments on theme***

* **Please share any final comments on the proposals in this theme below, including any areas that have not been covered or other proposals which you think should be considered.**

(open text box, 9,999 character limit, you can also upload supporting documents relating to this here.)

**Additional questions**

There are two supplementary questions included in the consultation

* **Theme 2: Opportunities for new process improvements and ways of working: What changes can we make to our processes to help reduce health inequalities in the way we develop our guidance, stakeholders participate and how health inequalities are identified and considered in making recommendations?**

(open text box, 9,999 character limit, you can also upload supporting documents relating to this here.)

* **Theme 4, Highly Specialised Technologies: Are there any areas where the vision does not address the needs of ultra-rare diseases?**

(open text box, 9,999 character limit, you can also upload supporting documents relating to this here.)

**Final comments on consultation**

After all four themes have been considered there is an opportunity to share final comments.

* **Please share any final comments on the consultation here:**

(open text box, 9,999 character limit, you can also upload supporting documents relating to this here.)

**About FPM and the context for our submission**

We are the Faculty of Pharmaceutical Medicine (FPM) ([www.fpm.org.uk](http://www.fpm.org.uk)), a charity and professional membership body on a mission to advance the science and practice of pharmaceutical medicine.

We set the highest scientific and ethical standards to help unlock the full potential of new medicines and make sure they are as safe as possible for patients.

We provide a collective voice for our 1,500 members who are striving to advance the research and development of new medicines to help prevent and overcome diseases that impact on the lives of patients worldwide. They are all medically-qualified and employed within the pharmaceutical industry, research organisations, drug regulatory authorities – or working as independent consultants.

Our mission is to advance the science and practice of pharmaceutical medicine by working to develop and maintain competence, ethics and integrity and the highest professional standards in the specialty for the benefit of the public.

This response has been prepared by the FPM’s Expert Groups (<https://www.fpm.org.uk/policy-and-publications/expert-groups/>) and Policy and Communications Group, both comprised of Members and Fellows of FPM – pharmaceutical physicians – doctors who are involved at every stage of the drug development pipeline, using their expertise to advance pioneering medicines, devices and diagnostics and ensure they are effective for patients.

FPM and ergo this submission is made independently from company and trade body influence and, in line with our charitable aims, focuses on patients, value for money and science and in supporting life sciences research.

**General comments on the outlined proposals**

Overall, FPM is supportive of the general principles outlined in the proposals:

* Alignment and efficiencies across programmes where diagnostics, devices and digital health/innovative technologies are assessed.
* Limiting number of meetings and length of times for assessment.
* Acknowledgement of some of the challenges for assessment of rapidly changing technologies such as digital health and genomics, and interest in developing specific guidance for these.

We would urge NICE to bear in mind the following:

* The more limited impact of a positive NICE appraisal for diagnostics, devices and innovative technologies vs therapeutics. For example, with diagnostics there is a huge opportunity to strengthen the uptake of innovative technologies by strengthening requirements to take up approved technologies, rather than just NICE providing implementation support. There should also be clear guidance and process for co-approval of therapeutics and companion diagnostics.
* We recommend that NICE consider the need for increased transparency from all stakeholders on decisions (including the rationale for access restrictions) and levels of prices for (ultra)-orphan products.
* We would encourage the optimal development of novel efficacy endpoint parameters in keeping with the regulatory accepted endpoints in particular related to immuno-oncology drugs, changing predominantly the tail of the survival KM curve rather than more short term response rate endpoints.
* Provide clear guidance on the utility and HTA acceptability of outcome data (inc PRO data) from oncology drugs on the EAMS program to support HTA access.
* FPM would encourage NICE to specifically address how they are going to ensure efficient assessment of companion diagnostic (CDx) tests that are required for the safe and efficacious delivery of new drugs. This is going to be increasingly the situation, particularly in rare diseases, where a population is often identified by genetic testing. Strategies for accelerated approval will make this particularly problematic as there will be two parallel HTA assessments (CDx and drug).
* FPM would encourage shared assessments or reduced processes where approved in England or devolved nations to reduce replication and/or that NICE and HTA systems across the UK consider moving towards a pan-UK system.
* WRT para 4: We agree that following Brexit and the Transition Period, this review presents a good opportunity to engage earlier in both setting the direction of development plans with value, outcome and effectiveness aspects built into these plans, rather than bolted on. It is important that there is harmonisation of data standards across GB (and hopefully UK) and that these standards are adopted more widely through EUNetHTA and ICER, to have an ICH-like approach to the data requirements even in the context of local cost and value decisions.
* WRT para 6: We agree on the success of programmes and the need for collaboration and cooperation, but we believe HTA should be simultaneous with issuing the MA and needs early partnership and engagement as well as use of binding indicators of value assessment that determine the value of the agreed outcome measures based upon the extent of the benefit at the time of approval and over time as benefit (or not) is further demonstrated. Flexible pricing / patient access schemes may assist this if based on clear measures and the value associated with the magnitude of their outcomes (links to Para 10 comment below).
* WRT para 10: FPM would recommend adding the need to flexibly allow for re-evaluation of cost effectiveness based upon evolution of the overall evidence base over time. This would allow value to be sustained and price (possibly by variable discounting up or down off a list price) to be rapidly amended to reward new data or increase discount if not positive. Pre agreed scales and assessments would allow this to happen more quickly.
* WRT para 20: We would recommend that NICE consider setting a target for time to patient access.
* WRT para 21: We would recommend that NICE have flexibility to consider novel models of value that assess lifetime value of the outcome delivered by a technology that may be given only for a very short period (when very high cost could be incurred) but the value is prolonged.
* WRT para 24: NICE should be encouraged to assess any digital health product for patients/clients with regard to their specific disease related monitoring/interactive function.
* WRT para 28: Whilst we understand it may have changed, although CDF did increase access more quickly, it was not matched with data collection from these new uses. Ensuring ongoing data collection and evaluation must be linked to any such access.
* WRT para 42: We agree in principle with increasing the charge to companies, as long as does not negatively impact their growth duty for SMEs and start-ups, as well as early academia spin out engagements, so there is a level playing field for all innovators regardless of origin, while encouraging UK start up and investment.