BIA comments on the draft HRA-MHRA Inclusion and Diversity Guidance

Q1 In what capacity are you answering this survey?

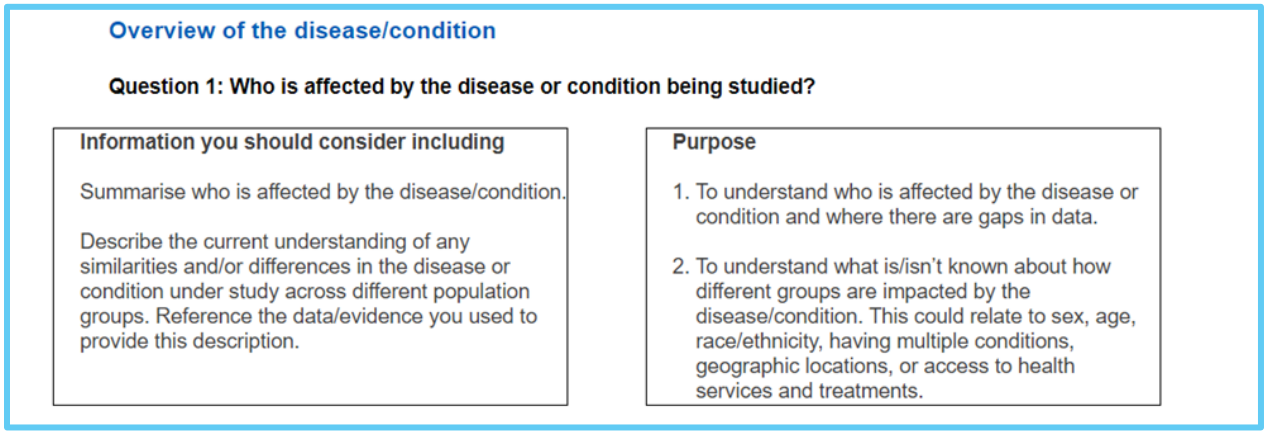
- **As an organisation**
- **The BioIndustry Association (BIA) is the voice of the innovative life sciences and biotech industry, enabling and connecting the UK ecosystem so that businesses can start, grow and deliver world changing innovation. The BIA represents 600+ biotech and life science companies, from start-ups to big pharma, as well as academic institutions, research organisations, charities and service providers to the sector.**

Q2 Please select which of the following would best describe yourself:

- **Member organisations develop research proposals / protocols**

Q3 Please tell us which area you live?

- **England, Northern Ireland, Scotland, Wales**



Overview of the disease/condition

Question 1: Who is affected by the disease or condition being studied?

Information you should consider including	Purpose
Summarise who is affected by the disease/condition. Describe the current understanding of any similarities and/or differences in the disease or condition under study across different population groups. Reference the data/evidence you used to provide this description.	1. To understand who is affected by the disease or condition and where there are gaps in data. 2. To understand what is/isn't known about how different groups are impacted by the disease/condition. This could relate to sex, age, race/ethnicity, having multiple conditions, geographic locations, or access to health services and treatments.

Q4 Is the purpose clear?

- **Yes**

We understand the purpose and agree with the principles in general that it is desirable to include a diverse population in clinical trials.

Q5 Is the question clear?

- **Yes**

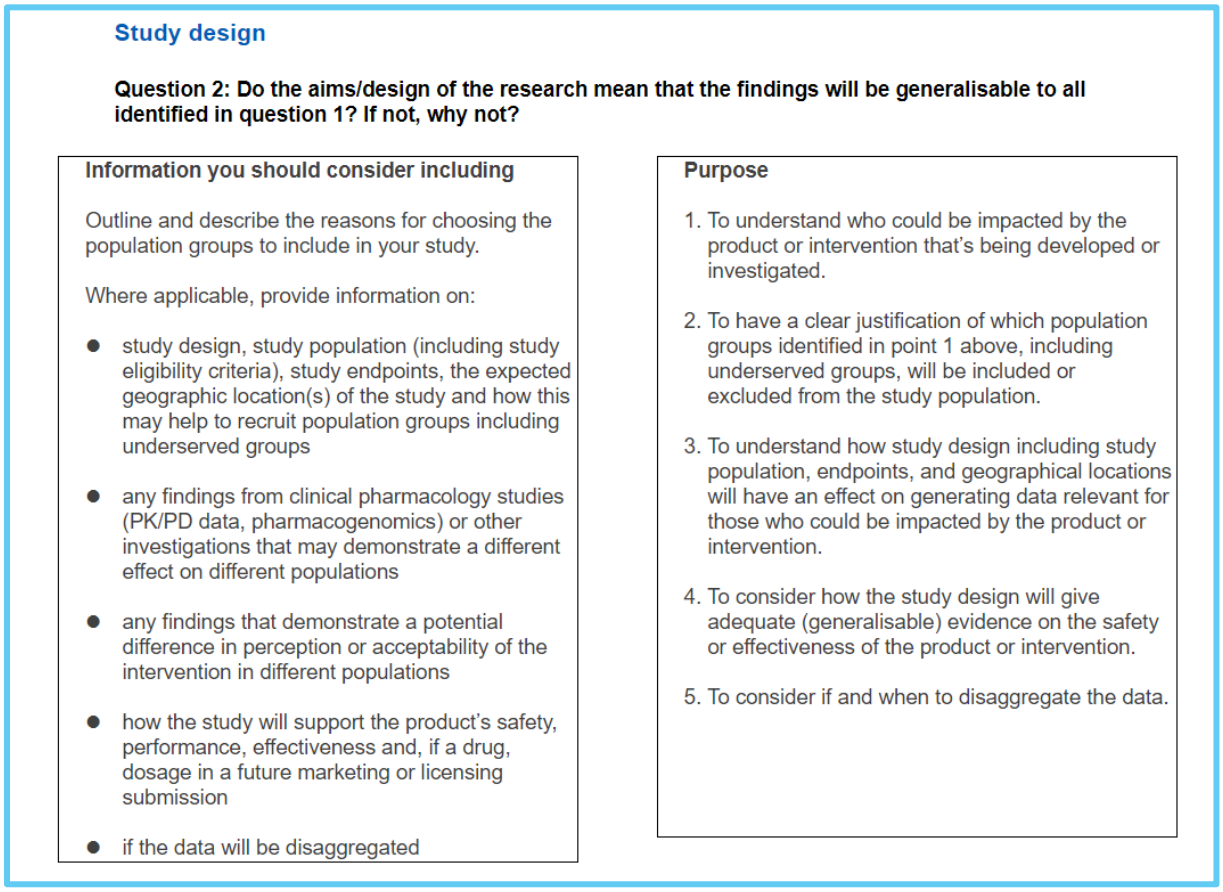
Whilst sex, age, race/ethnicity, multiple conditions and geographic location may be recorded when capturing demographics as part of the Case Report Form (CRF), we believe it is neither possible nor ethical to capture some of the factors, particularly given their potential discriminatory effect on certain specific layers of the wider population when developing the Inclusion & Diversity Plan, such as those being postulated e.g., status on access to health services and treatments, neurodiversity, sexual orientation, homelessness, faith, income at the time of recruitment. Such socio-economic considerations may have a bearing on the individuals' willingness or attitudes to participate in clinical research, and disease predisposition as well as influence on health outcomes. That said, these considerations cannot be universally applied and will require a case-by-case approach to be adopted, taking account of the nature of medical interventions, the conditions for which the intervention is being investigated and the relevance of such considerations in the context of the study. It is also worth mentioning that openness for capturing additional factors requires considerable educational programs (if people would understand why some factors are captured and the reasoning is clear for them, they may open for data capturing). We would also like to emphasise that companies run global trials, with greater reliance on a harmonised and standardised study protocol to inform the final data analysis, and such aspects may vary considerably across countries and regions, which makes it even more practically challenging for such a priori considerations to be implemented.

- **For multinational studies the guidance advises that the plan should state the overarching study wide recruitment goals and explain how the UK study will contribute to them. Further clarification and guidance on expectations for goal setting in multi-regional clinical trials i.e., UK vs. global targets would be supported in addition to how non-UK participants factor into enrolment goal setting. Intersectionality should be taken into account when considering underlying reasons as to why certain patients may be underrepresented in clinical trials and how multiple forms of inequity and disparities may provide challenges when enrolling underrepresented and underserved groups in clinical trials.**
- **The terminology used to describe race and ethnicity differs among countries as do data collection and data use practices. Therefore, it is important to define key terminology in the guidance to work towards long-term international harmonisation.**

Q6 What are the potential challenges in answering this question?

- **Potential divergence with the FDA guidance, which focuses on age, ethnicity, sex and race, since multi-national trials would complete the FDA diversity action plans before reaching this stage in the UK.**
- **It would be helpful to clarify what would be the HRA and MHRA expectations in cases where there is no epidemiological data/sub-group data available in the specific disease/condition prognostic of clinical outcomes particularly in**

circumstances where there are significant gaps in the understanding of the presentation of the disease or condition (e.g. rare diseases; paediatric indication).



Study design

Question 2: Do the aims/design of the research mean that the findings will be generalisable to all identified in question 1? If not, why not?

Information you should consider including	Purpose
Outline and describe the reasons for choosing the population groups to include in your study. Where applicable, provide information on: ● study design, study population (including study eligibility criteria), study endpoints, the expected geographic location(s) of the study and how this may help to recruit population groups including underserved groups ● any findings from clinical pharmacology studies (PK/PD data, pharmacogenomics) or other investigations that may demonstrate a different effect on different populations ● any findings that demonstrate a potential difference in perception or acceptability of the intervention in different populations ● how the study will support the product's safety, performance, effectiveness and, if a drug, dosage in a future marketing or licensing submission ● if the data will be disaggregated	1. To understand who could be impacted by the product or intervention that's being developed or investigated. 2. To have a clear justification of which population groups identified in point 1 above, including underserved groups, will be included or excluded from the study population. 3. To understand how study design including study population, endpoints, and geographical locations will have an effect on generating data relevant for those who could be impacted by the product or intervention. 4. To consider how the study design will give adequate (generalisable) evidence on the safety or effectiveness of the product or intervention. 5. To consider if and when to disaggregate the data.

Q7 Is the purpose clear?

- **Yes**

We recognise the importance of inclusion and diversity in clinical trials to improve insight into the determinants of variability in the treatment response so that all communities can benefit from scientific advances. Such a policy ought to be thoughtfully implemented having regard to the stage of the clinical development and the overarching study objective and the scientific questions to be addressed, to minimise delay in decision-making on progress of clinical development. For early-stage clinical development, the scientific question is narrowly centred around whether the experimental treatment has an effect in humans instead of data generalisability, therefore the approach must be balanced. Nonetheless, sponsors should be mindful of the principles of inclusion and diversity early in development to enable having a representative population (including underserved groups) of the

target disease as early as possible and no later than late phase development. This would align with US guidance and therefore support sponsors with global product development.

Q8 Is the question clear?

- **Yes**

Q9 What are the potential challenges in answering this question?

- **Gathering information on patient perceptions and the acceptability of the intervention will likely rely on small focus groups conducted by patient organisations at a global level.**
- **It is unlikely that direct engagement with patients in the UK can be achieved for each study, making global data or insights from these focus groups the primary source of information, due to limited lead time and resources.**
- **Additionally, multinational trials complete the FDA diversity action plans before reaching this stage in the UK (therefore, the HRA and the MHRA should consider aligning with these requirements).**

Study goals

Question 3: What are your recruitment goals?

Information you should consider including	Purpose
Specify the goals for recruitment of population groups outlined in question 2. Outline and provide the rationale for planned recruitment of participants based on the information provided in Question 2.	1. Consider what goals can be set to recruit the proposed population groups, particularly underserved groups. 2. Decide whether increased recruitment of a population is required to identify differences.

Q10 Is the purpose clear?

- **Yes**

As reflected in the response to question 5 above, it could be challenging to capture status for some of the underserved groups.

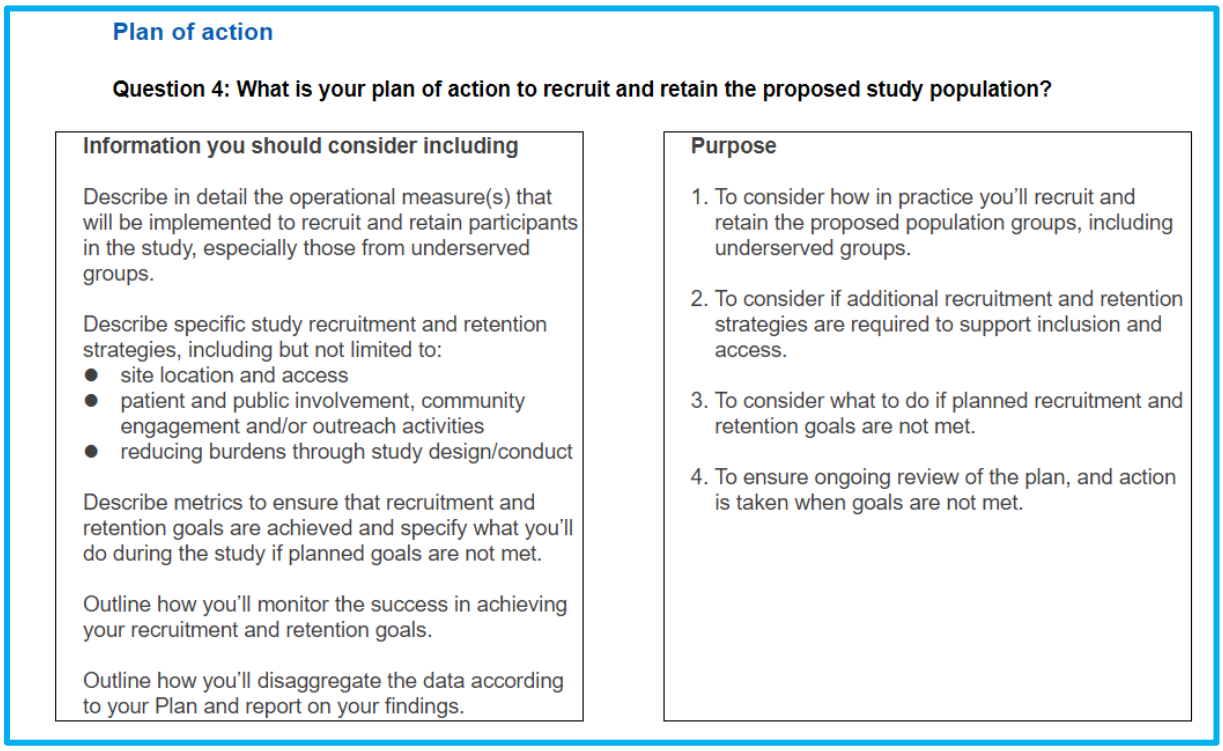
Q11 Is the question clear?

- **Yes**

Q12 What are the potential challenges in answering this question?

Please refer to challenges captured in the responses above. It could also be challenging to:

- **identify recruitment targets for some of the sub-population even if there are epidemiological data for them (rare diseases, paediatrics); and**
- **set recruitment strategies and targets for large multi-national trials, since they are dictated at a global level rather than country level.**



Plan of action

Question 4: What is your plan of action to recruit and retain the proposed study population?

Information you should consider including	Purpose
Describe in detail the operational measure(s) that will be implemented to recruit and retain participants in the study, especially those from underserved groups. Describe specific study recruitment and retention strategies, including but not limited to: ● site location and access ● patient and public involvement, community engagement and/or outreach activities ● reducing burdens through study design/conduct Describe metrics to ensure that recruitment and retention goals are achieved and specify what you'll do during the study if planned goals are not met. Outline how you'll monitor the success in achieving your recruitment and retention goals. Outline how you'll disaggregate the data according to your Plan and report on your findings.	1. To consider how in practice you'll recruit and retain the proposed population groups, including underserved groups. 2. To consider if additional recruitment and retention strategies are required to support inclusion and access. 3. To consider what to do if planned recruitment and retention goals are not met. 4. To ensure ongoing review of the plan, and action is taken when goals are not met.

Q13 Is the purpose clear?

- **Yes**

Recruiting/retaining some patients in certain populations may be impractical. For example, homeless or travellers may not be recruited in clinical trials as the follow up may be impractical.

Q14 Is the question clear?

- **Yes**

Q15 What are the potential challenges in answering this question?

It is more challenging to monitor recruitment/retention of some sub-populations (e.g., faith, economic status are not captured, and we believe it may be seen as unethical or otherwise potentially discriminatory).

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Q16 **Do the questions give you an opportunity to include information you would not generally provide or receive in a submission?**

- **Yes, the questions gave us the opportunity to highlight a specific population where the disease is more prominent in.**

Q17 **Do you think the questions will have a positive impact on the design of studies by helping researchers to develop more inclusive protocols?**

- **Yes, this should encourage everyone to reflect on those aspects.**

Q18 **Having read the supporting guidance, I have the information I need to create an Inclusion and Diversity Plan.**

Do you agree with this statement?

- **Yes, we appreciate the opportunity to receive further guidance to support inclusion and diversity as well as understand findings that may emerge from the pilot program. The use of case studies may facilitate the understanding of the intent behind the guidance.**
- **While we anticipate an improved representation of underserved populations in clinical trials, we recognise it might be challenging to make an impactful difference in some populations, for which the population is already limited, for example rare diseases or paediatric indications.**
- **Inclusion and diversity requirements should be carefully adjusted – particularly concerning the implementation and challenges of inclusion and diversity in clinical trials, since unnecessary delays in the approval and execution of early-stage clinical development are not in the interests of patients and public health.**

Q19 **Is there anything missing from the guidance or do any sections need more detail?**

- **Yes, we would appreciate more details to support greater understanding of how the pilot will function and align with other jurisdictions:**
    - **What form of training or required knowledge will the REC members have on clinical trial diversity and health equity to be qualified reviewers of these plans?**
    - **Information on submission and review timeline with the REC, including scenarios where the REC may have comments or questions and potential impact (if any) on the timelines associated with the clinical trial application process.**
    - **Information on timing/planning of scientific advice meetings.**
    - **It would be helpful to understand the HRA-MHRA thoughts about the UK requirements in the context of regulatory requirements in other jurisdictions since maximising alignment as far as possible would be desirable. Will the HRA and the MHRA take the FDA (and any other major**

regulators views on this topic) into account before finalising the UK guidance and plan?

- **We would recommend providing some examples of completed plans which would be helpful for industry to present pilot findings in a template format.**
- **Regular exchange on best practice and examples of successful implementation would also be helpful.**