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Online Supplementary appendix. Detailed method of the consultation

On October 2021, the *Haute Autorité de santé* (HAS) was asked by the French Ministry of Health to elaborate recommendations on the methodological challenges associated to accelerated clinical developments.

1. Constitution of an expert committee

An expert committee of 23 members was constituted with permanent members of HAS and experts outside of the institution. External experts were directly contacted by HAS for their academic expertise in biostatistics, methodology for clinical research, pharmacology, or clinical expertise. They have filled a standardized form listing potential conflict of interests which was published on a governmental website publicly accessible (https://dpi.sante.gouv.fr/dpi-public-webapp/app/home).

A first gathering of all the members of the committee has taken place on October 28th, 2021, to introduce the problematic and conduct of the consultation.

2. Auditions of relevant stakeholders by the expert committee

From November 2021 to January 2022, various stakeholders' representatives were auditioned by the expert committee. They were directly contacted by HAS. Several days before the audition, the broad problematic of the methodological challenges associated to accelerated clinical developments was introduced to them, and a conductor in the form of a brief questionnaire (see section 7 below) was proposed to help structuring their presentation during the audition.

Six auditions of representative members of one institution were conducted (approximatively one hour long each). Each institution was free to choose the persons who were auditioned. During these auditions, each institution was invited to first deliver the messages they wanted to the expert committee. Then, there was the conduct of an open discussion with the members of the expert committee.

The institutions that were auditioned were:

- "Les entreprises du medicament" and "France Biotech": representatives of the manufacturers in France,

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- "La conference nationale des CPPs", representatives of the ethics committees in France,
- Academics from the "Assistance Publique – Hôpitaux de Paris" (University Hospital of Paris),
- "Le Groupe des Associations de Malade de l'Inserm" and "France Assos Santé", representatives of the users of the health system in France.

Three auditions on a specific theme with several institutions invited at once were conducted (approximatively two hours long each).

An audition on oncology was conducted with:

- The oncology department of the "Agence Nationale de Sécurité du Médicament et des produits de santé", the French regulatory body,
- "L'institut national du cancer" (INCa), the French national institute for cancer research,
- "UNICANCER", a French federation of major cancer treatment centres,
- "Patients en réseau", patients' représentatives,
- "La ligue contre le cancer", a non-governmenta organization promoting cancer research in France.

An audition on rare diseases was conducted with:

- The rare disease department of the French ministry of health,
- "OrphanDev", a national network for clinical research for rare diseases,
- "Eurordis", patients' representatives in Europe,
- The center for clinical research for rare diseases of Lyon (University of Lyon).

An audition on in silico methodology and artificial intelligence was conducted with:

- Novadiscovery, contract research organization,
- Owkin, contract research organization,
- ARIIS, a network for clinical research.

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3. Public consultation

During the whole month of November, a public consultation was organized by HAS. The public consultation was available through a public website. The public consultation was advertised through press coverage and massive e-mailing.

Any person interested was invited to complete an online, short, unspecific, and open questionnaire regarding the problematic of the methodological challenges associated to accelerated clinical developments (the questionnaire is available below, see section 7). The public consultation was available in French and English, but only contributions from French stakeholders were received.

4. Synthesis of the audition and public consultation

An internal qualitative non-systematic synthesis of all the auditions and all the received public consultation (50 answers) was performed by permanent members of the HAS from November 2021 to January 2022. Supports used by presenters during each audition (such as slide decks or other types of documents) were systematically recovered. During each audition, notes were taken by one member of the HAS. After each audition, a synthesis was written and sent to all the members of the expert committee. After closing of the public consultation, responses were classified into recurring themes and the occurrence of the themes were quantified. A synthesis of the public consultation was written and sent to all the members of the expert committee.

5. Definition of a specific problematic to be addressed

All the members of the expert committee were gathered for a meeting that has taken place on January 25th, 2022. A qualitative synthesis of the auditions and public consultation was restituted followed by an open discussion between the members of the expert committee. At the end of the meeting, the problematic tackled by the current manuscript was finally selected by weighting the initial request of the French ministry of health against the qualitative results of the synthesis of the auditions and public consultation.

6. Endorsement of the problematic by the board of HAS

The focus and problematic prioritized was validated by the board of HAS.

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7. Online questionnaire that was used for the public consultation.

Where are you from?

- Academic world (e.g., research lab, university, university hospital)
- Academy of health professionals
- Health professionals' order
- Health Technology Assessment body
- Industry / CRO / Consultant
- Learned or scientific society
- Patients' representative
- Professionals' union
- Other: Specify

Name of your organization:

E-mail:

Does your contribution is endorsed by your organization?

- My contribution is endorsed by my organization
- I contribute on my behalf

1. **Are there specific methodological issues for Health Technology Assessment you wish to bring to our attention?**

2. **Do you identify methodological issues relative to the assessment of innovative drugs in specific therapeutic areas?**

3. **To accelerate the access to innovative drugs, what could be useful clinical trial designs or methodological specificities?**
   - What are the strengths and weaknesses of these approaches?
   - What are the opportunities and threats to the use of these approaches?

4. **To accelerate the access to innovative drugs, how the HAS could modify its methodology for Health Technology Assessment?**

5. **Do you have any additional comments?**

6. **How did you proceed for answering to the questionnaire?**
   - What are the types of sources you used? (e.g., personal experience, survey, social networks, teamwork, testimony, scoping review, expert's opinion)

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Please, summarize your contribution

- Please, list the bullet points of your contribution

What are the relevant references you used to answer the questionnaire?