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Client Alert

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EUROPE – New Interim Guidance on Parallel EMA-HTA Body Scientific Advice

On July 3, 2023, the European Medicines Agency ("EMA") and the European Commission published a Guidance on Parallel EMA/HTA body Scientific Advice for the Interim Period ("Guideline").

The Guideline organizes parallel scientific advice ("PSA") by the EMA and national health technology assessment bodies ("HTAb") on a rolling basis, for the period between September 2023 and January 2025 when the European Union ("EU") Regulation 2021/2282 on health technology assessment ("HTA Regulation") becomes operational. It explains the eligibility criteria, timelines, and procedure, as well as the role and responsibilities of each participating party.

Generally, opportunities to receive scientific advice are increasing in the EU. In February 2023, the EMA organized a pilot project for high-risk medical devices by the expert panels created by the Medical Devices Regulation ("MDR"). In November 2022, the Heads of Medicines Agencies ("HMA") launched the second phase of their pilot project on simultaneous national-level scientific advice.

GENERAL DESCRIPTION

Parallel or joint EMA-HTAb scientific advice is not new. It was set up about 10 years ago on an informal basis, regularly evolved, and largely contributed to the adoption of the HTA Regulation. Since then, parallel scientific advice has been replaced by pilot applications of the HTA Regulation, each with a limited application period. The Guideline in essence provides for a new pilot but on a rolling basis for about 16 months.

Like the previous parallel scientific advice schemes, the interim PSA will provide scientific advice on initial evidence generation so that pharmaceutical companies can design their trials and generate data to adequately support not only their marketing authorization applications but also their pricing and reimbursement applications and Post Licensing Evidence Generation ("PLEG").

ACTORS

The EMA and the HTAbs have specific roles and responsibilities.

EMA – The EMA participates in the PSA through its Scientific Advice Working Party ("SAWP"), which provides general, regulatory-only scientific advice (advice on tests and trials necessary to demonstrate the quality, safety, and efficacy of medicinal products) when only the EMA is involved.

HTAbs – National HTAbs may, at their discretion, participate or not in a PSA. If an HTAb decides to participate, it may do so either (i) as an active participant, providing advice based on its national HTA requirements, or (ii) as an observer.

A minimum of two active HTAbs is required for each PSA. If fewer than two HTAbs are available after the selection process, the PSA continues as a simple regulatory-only EMA scientific advice.

A company may not choose the HTAbs to be involved in its PSA.

HTA Coordination Contact – The G-BA (Gemeinsamer Bundesausschuss/Federal Joint Committee, Germany) is designated as the HTAbs Coordination Contact for centralized recruitment and practical coordination of participant HTAbs.

Associated Experts – The EMA or the HTAbs may decide whether to involve healthcare professionals/clinical experts and patient representatives in their respective assessments.

PRODUCT SELECTION CRITERIA

Request for Participation – Companies can apply for PSA from September 2023 until January 2025, by submitting an application form and its annexes to the EMA and the HTA Coordination Contact. The HTA Coordination Contact will notify the company and the EMA about the outcome of the selection within 4 weeks.

Selection Criteria – Not all medicinal products may benefit from PSA. First, the pivotal clinical trial (pivotal phase II/ or III) must not have started yet. Second, the product must meet selection criteria that are identical to those of the HTA Regulation since the interim PSA prepares the joint work of EMA and HTAbs for joint scientific consultations under the HTA Regulation:

- unmet medical need (no treatment or only unsatisfactory treatment available);
- first in class;
- potential impact on patients, public health, or healthcare systems;
- significant cross-border dimension;
- major EU-wide added value; or
- EU clinical research priorities.

Priority is given to oncology products, advanced therapy medicinal products ("ATMPs"), and indications for which there is no established guidance for clinical development (i.e., in an absence of recent HTA evaluation in a similar indication).

The final selection will depend on each HTAb's available resources.

PROCEDURE

The PSA procedure comprises several phases: pre-submission, submission, evaluation, and 'decision'.

Application – Applications must be complete, i.e., address all relevant questions, because no follow-up consultation is envisaged. The company may amend its development plans, provided that it informs all parties involved before the discussion meeting (specific deadlines) and sends a clear comparative table of the changes and their justification. Yet, substantial changes have to be communicated to the EMA at least 5 working days, and to the HTAb at least 12 working days, before the discussion meeting, respectively.

Pre-submission – The company must submit its application and draft briefing package to the EMA and the HTA Coordination Contact at least 30 days before the start of the procedure so that it has enough time to clarify and answer questions and to finalize the briefing package. The EMA will confirm the date and time of the discussion meeting (see below).

Submission – After validation of the application by the EMA, the company submits the final briefing package to the EMA and the HTA Coordination Contact, which will forward it to the participating HTAbs.

Evaluation – The consultation/evaluation takes the form of a discussion meeting that allows direct exchanges between the parties involved (EMA, HTAbs and company).

Lists of Issues -- Before the discussion meeting, two lists of issues indicating the focus and issues of the EMA and the HTAbs are prepared and discussed between the EMA and the HTAbs. The lists are then communicated to the company so that it can send written responses before the discussion meeting (specific deadlines).

Of note, there is no assessor for HTA – each HTAb is responsible for its recommendations and provides its national position individually. Yet, the PSA implicitly seeks consensus.

Discussion Meeting --The (currently virtual) discussion meeting is hosted by EMA and is co-chaired by the EMA and one of the HTAbs. The objectives of the discussion meeting are:

- To discuss issues of concern or disagreement from EMA and/or HTAbs with the Applicant's proposal regarding major aspects of trial designs.
- To get a mutual understanding of each body's constraints as it has to be acknowledged that Regulators and HTAbs are operating within distinct remits (benefit/risk evaluation vs. added value or cost-effectiveness evaluation). Possible resulting divergences between Regulators' and HTAbs' positions on major aspects of the trial design will be discussed.
- To share and discuss preliminary positions on major aspects of trial designs from HTAbs with all participants.
- To discuss potential solutions that could facilitate one trial design or at least one development plan.

Timeline – Applications must be submitted 3 months before the start of the procedure. The Guideline includes a detailed timetable for the PSA procedure.

OUTCOME

At the end of the PSA, which should normally last 3 to 5 months, the company receives:

- a scientific advice letter from the EMA. As currently is the case, the scientific advice is not legally binding but, in practice, it is taken into consideration during the marketing authorization procedure and the company must justify any deviation therefrom.
- individual written recommendations from each participating HTAb. Importantly, the individual recommendations only reflect the state-of-the-art of medical science and national requirements at the time of advice.

CONFIDENTIALITY

The PSA process is confidential, and companies implicitly agree to the exchange of information between the EMA, the participating/observing HTAbs, and the associated experts, all of which are bound by confidentiality agreements.

OTHER TYPES OF SCIENTIFIC ADVICE

Simultaneous National Scientific Advice ("SNSA") – National competent authorities ("NCAs") provide scientific and/or regulatory advice at different stages of development, based on national rules and requirements. Where applicants seek advice on the same set of questions and data package (on scientific and/or technical-regulatory issues) from two different NCAs, they may apply for a SNSA. Applicants select two NCAs from the participating NCAs, and one of them takes the lead of the procedure. Feedback by the Clinical Trial Coordination Group (the HMA's working group on clinical trials) can also be provided under the SNSA, provided that the participating NCAs consider it useful. The scope of the SNSA is limited to medicinal products and drug-device combination products. In practice, this phase of the SNSA focuses on multi-country clinical trial applications.

EU – U.S. Scientific Advice – Applicants interested to receive scientific advice from both the EMA and the United States Food and Drug Administration ("FDA"), may apply for an EMA-FDA parallel scientific advice. The program helps sponsors to obtain scientific advice and protocol assistance on scientific issues during the development phase of new medicinal products. The objective is to exchange information, increase early dialogue between companies and both regulators, deepen the understanding of relevant regulatory decisions and divergences, and optimise product development by avoiding unnecessary duplication. Each Agency retains its autonomy, and their independent final advice may still differ after the joint discussion. Yet, the aim is to provide convergent advice.

Combination Products – Since February 2023, the EMA is running a pilot project that enables expert panels (set up by the MDR to strengthen the assessment of high-risk medical devices) to provide scientific advice to EU manufacturers of class III devices and class IIb active devices intended to administer and/or remove a medicinal product from the human body. Devices intended to treat a relatively small group of patients (e.g., "orphan devices" and devices for paediatric use), devices for unmet medical needs and novel devices that have a possible major clinical or health impact are prioritized. Submission of letters of interest are possible until August 2023.

In addition, combination products fall under the scope of national scientific advice in some Member States and of the SNSA.

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Companies involved in the development of medicinal products and interested in PSA should prepare their applications and be ready to submit them sooner rather than later, as HTAbs' resources will slowly be monopolized by previous applications.

King & Spalding's regulatory Life Sciences lawyers can help you better understand the Parallel Scientific Advice interim program in order to prepare for and participate in this new program beginning in September 2023. Our team closely monitors regulatory developments on scientific advice and parallel scientific advice and will keep you updated.

ABOUT KING & SPALDING

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