

Section 4: Strategy for Continuous Provision of Scientific Resources for Medicine Assessment

1. Objective

To identify and ensure access to the best scientific expertise and evidence to support robust regulatory decision making by the network of European Medicines Agencies.

2. Current assets in terms of scientific resources and the organisation of access to these resources

2.1 Experts

2.1.1 Staff working in regulatory Agencies

2.1.2 People external to competent authorities (science, academia, and health professionals)

It should be realised that there is a considerable complexity in the review structure of EU member states. Models vary between

“a Body comprising mostly (academic and health-care) experts to assess full dossiers for a mostly administrative authority comprising civil servants”

to

“a regulatory agency with full-time scientific assessors responsible for the review (perhaps with the possibility to discuss concrete, specific questions with external experts)”

representing the extremes.

It should be taken into account that all these models (developed mostly by tradition) do work! It means that the regulatory model itself may not be decisive, i.e. advocating (even indirectly) solutions that are specific for one single regulatory model is not appropriate. Some issues, however, e.g. overcoming conflicts of interest, may need solutions specific to the regulatory model.

2.2 Information resources e.g. population health databases

2.3 Facilities such as analytical and research laboratories

2.4 Other organisations in the scientific/public health arena

Better visibility of the access to these different categories of resources per member state competent authorities should be organised. (E.g. the external experts circle used by national competent authorities is much wider than is listed by EMEA, existence of and access to national health databases, possession of or prompt access to different laboratories, their expertise, etc.).

The group feels that a survey on the actual assets of scientific resources for competent national authorities in the member states would be of value, in particular in understanding how experts are used. In line with the concept of a EU network, it is suggested that, when certain expertise is not available, expertise could be sought in another Member State via the relevant competent authority.

3. Developing the actual scientific resources for optimal regulatory decision making now and ensuring future regulatory needs are met as science evolves

There are three basic components of the optimal regulatory decision making:

- scientific (academic) knowledge (inevitable),
- interdisciplinary approach (needed),
- clear understanding of regulatory affairs (important!).

The first component is self-evident. One must have a deep academic knowledge to review MA

dossiers. (Only to *understand* the issues is *not enough!*) This kind of knowledge can only be accumulated by intensive scientific work. Thus, at least academic background is needed. The issue is how to

- ensure more learned people to work (internally and externally) for the regulatory authority?
- evaluate how “learned” they are (for scientific degrees or scientometry are not adequate for this purpose).

The second above bullet is connected to the interdisciplinary approach. One cannot assess, e.g. the quality, nonclinical and clinical parts of a marketing authorisation dossier in isolation. There may be information in one part that has consequences in another. (E.g., evaluation of a toxicology module starts with checking whether the impurity profiles of the sample used and those in the final specification are the same, a step that is rarely taken by academic toxicologists. Moreover, apart from medical knowledge, methodological/statistical expertise is also needed, for the assessment of pharmacological results, pharmacokinetic expertise should also be available, etc.)

The issue is how to generate this special feeling for interdisciplinary (i.e. to have knowledge in another disciplines, deep enough to identify possible connections). One should not forget that, at present, the “academic approach” is mostly the opposite: “deep knowledge in a narrow branch of sciences” is “scientometrically” much more “profitable”, ensuring publication of series of papers in journals of high impact and citation!

Lack of the third component, i.e. understanding regulatory affairs, may pose unexpected problems. According to the “pure” academic approach (naturally, taken the extremes):

- formalities (laws and regulations), as well as procedural details (“bureaucracy”) are not interesting for scientists,
- deadlines are far less important than scientific merit,
- persons with more learned degrees tend to be right,
- statements of esteemed Scientific Boards may not be challenged,
- “mutual recognition” of others’ review is beyond the scientific approach.

By contrast, the regulatory approach understands that

- there are procedures when unmet deadlines mean that your opinion is not taken into account,
- any opinion, statement, etc. can be challenged, you must always possess good arguments to defeat your opposition,
- compromises (such as accepting others’ opinion you only partly agree with) are inevitable.

An additional point is that a medicinal product is rarely developed on its own. Regulatory and scientific memory is needed. Such memory consists of assessment of another products belonging to the same therapeutic area, former advices and guidance supporting development of such products or compounds given may also form the background for the assessment of a new product. There is a need to ensure that such knowledge is made available, also in the case of internal, but particularly for external assessors. This may be done by making these data available in one single EU database (e.g., that of the EMEA) but also experts participating in committees, working parties, ad hoc groups should be prepared to possess this knowledge or to report back such needs to their national competent authorities.

The best solution to overcome these issues is the adequate and continuous training of (both internal and external) assessors. It should include

- 3.1 Training of (mostly internal) assessors according to develop their skill (quality, safety, and efficacy) further.
- 3.2 Training of external experts to understand regulatory affairs.
- 3.3 Building links with academia so as to ensure regulatory provisions closely follow emerging science.

3.1 Apart from the international courses organised by EMEA and others, the group feels that identification and listing of other international and national education and training possibilities throughout the European Union would be of value. At present, such courses are provided by

academia (graduate and postgraduate level, diploma), professional organisations (e.g. pharma industry associations or regulatory affairs societies) and the national competent authorities themselves (from formal courses to in-practice training). Registration to and participation in these courses for the right regulatory experts are occasional and not prioritised. There should be a mechanism to identify and prioritise these courses as well as for funding participation of external experts.

3.2 Several authorities and other organisations developed informal and formal courses to describe regulatory affairs (both civil service rules and, e.g. the administrative flow of European MA procedures) for those academic and health-care professionals who serve the assessment as external experts. These initiatives should be structured, listed and offered for others (language permitting).

3.3 Initiatives of building links with academia so as to ensure regulatory provisions closely follow emerging science should be identified in different member states and structured to serve the needs of the network of European Medicines Authorities.

4. Identification of barriers and challenges in achieving the best scientific resources

4.1 The EU network of Agencies: its size and diversity (see 2.1.2) is a challenge in itself due to its complexity.

4.2 In the area of data resources (see 2.2), the sources of funding can be a barrier, uneven to the different member states. Further discussion within the European Commission about the need to earmark sources of funding is advocated.

4.3 Exclusion of conflict of interests (Col). Apart from the national solutions, there is the EMEA model for declaration of Col, supported by the requirements of *Article 126b* of the Directive 2001/83/EC. However, the issue is whether it is enough and if yes, how to understand them?

Particularly in smaller countries where there is no “flow of experts” in special scientific fields, the following questions may be raised:

- What the Col declaration mean? E.g. is a clinician that declared a potential Col (performing clinical trials for commercial sponsors upon payment) for the past expected to refuse conducting such trials in the future? If not, how long the Col declaration is valid?
- What if the regulatory expert’s spouse or dependent children have Col? (Remark: this may for many countries be partly covered in national laws on Col. but should be included in the discussion. However the most important issue is transparency on these matters.)
- What if the colleagues/co-workers of an external expert (e.g. in the same University Department) have a Col? (I.e. not the person but his Department benefits from the contacts with commercial sponsors?)
- Could experts leaving the pharma industry for the regulatory authority “independent” on the next day? (In some member states, there is a transition period, of e.g., one year. Within this time-frame, they are not allowed to work with applications, etc., from their former company, but are allowed to work with applications by competitors.)
- Can, e.g. a clinician just finishing a trial with one of the ACE inhibitors independent and reliable for assessing the next day the dossier of another ACE inhibitor?

The group feels that this issue, naturally, by careful comparison of the national laws and rules, should be elaborated to develop an EU Medicines Agencies Network wide guidance. It should be balanced for an indulgent solution makes the Col declaration ineffective while a too stringent one may hinder using the real expertise for regulatory purposes.

4.4 Selection criteria for experts need to be developed and published

The HMA is requested to develop such criteria.

4.5 Staff training systems are needed to support common standards, and staff exchanges would assist

See also 3.1 – 3.2. Such standards, specific for medicines assessors, should be identified.

4.6 Quality control systems also need to be developed

There should be systems, direct and indirect, harmonised throughout the EU, to control quality of the assessors.

5. Priority setting

Having the above recommendations accepted it would be important to identify short, medium and long term goals. For example,

5.1 a short-term goal may be better “visibility” of the assets of EU Medicines Agencies Network in terms of scientific staff. Creation of “skills database”, wider than that for EMEA experts, is recommended to facilitate contact between assessors of different disciplines, and selection of assessment teams for particular reviews.

5.2 A medium-term goal could be a focus on better use of public health databases.

5.3 A long-term goal could be to have a scope to Commission research to support best regulatory decision making, if funding streams are available.