Transparency: How Much is Too Much? – HTA perspective

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NICE National Institute for Health and Care Excellence

Why is transparency important?

Transparency is critical to public trust in evidence-based decision making in health and is a cornerstone of health technology assessment across the world

q ̲ VaIPvIIaư̲ ưø A : A multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system.... The process is formal, systematic and Ḧn âṅę ȟ âṖ, and uses state-of-the-art methods to consider the best available evidence.[1]

Across the world, others involved in HTA and regulation are demanding increased levels of transparency

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1. HTAGloassry.net. Health Technology Assessment. [HtaGlossary.net | health technology assessment]

Have we moved on since Tamiflu and Edronax … now more than a decade ago?

BMJ

BMJ 2014;348:g2263 doi: 10.1136/bmj.g2263 (Published 9 April 2014)

ANALYSIS

Multisystem failure: the story of anti-influenza drugs

Last year the Cochrane team, with the help of the *BMJ's* open data campaign, finally got access to full clinical study reports on neuraminidase inhibitors. **Tom Jefferson** and **Peter Doshi** explain what the new systematic review found and how a series of failures meant that decisions about these drugs were made without the full evidence

Tom Jefferson *reviewer*[1], Peter Doshi *assistant professor*[2]

[1]Cochrane Acute Respiratory Infections Group, 00187, Roma, Italy; [2]Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, USA

This article is more than **12 years old**

Antidepressant reboxetine no better than a placebo, study finds

Scientists accuse Pfizer of holding back studies which reveal drug sold as Edronax to be ineffective and potentially harmful

Pfizer has been accused by scientists of failing to disclose studies which show the inadequacies of reboxetine. Photograph: Timothy A Clary/AFP/Getty Images

An antidepressant prescribed in the UK over the last 13 years is ineffective and potentially harmful, according to a damning study published today.

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Yes, ‘we’ have …

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But, ‘it’ has come at a ‘price’ …

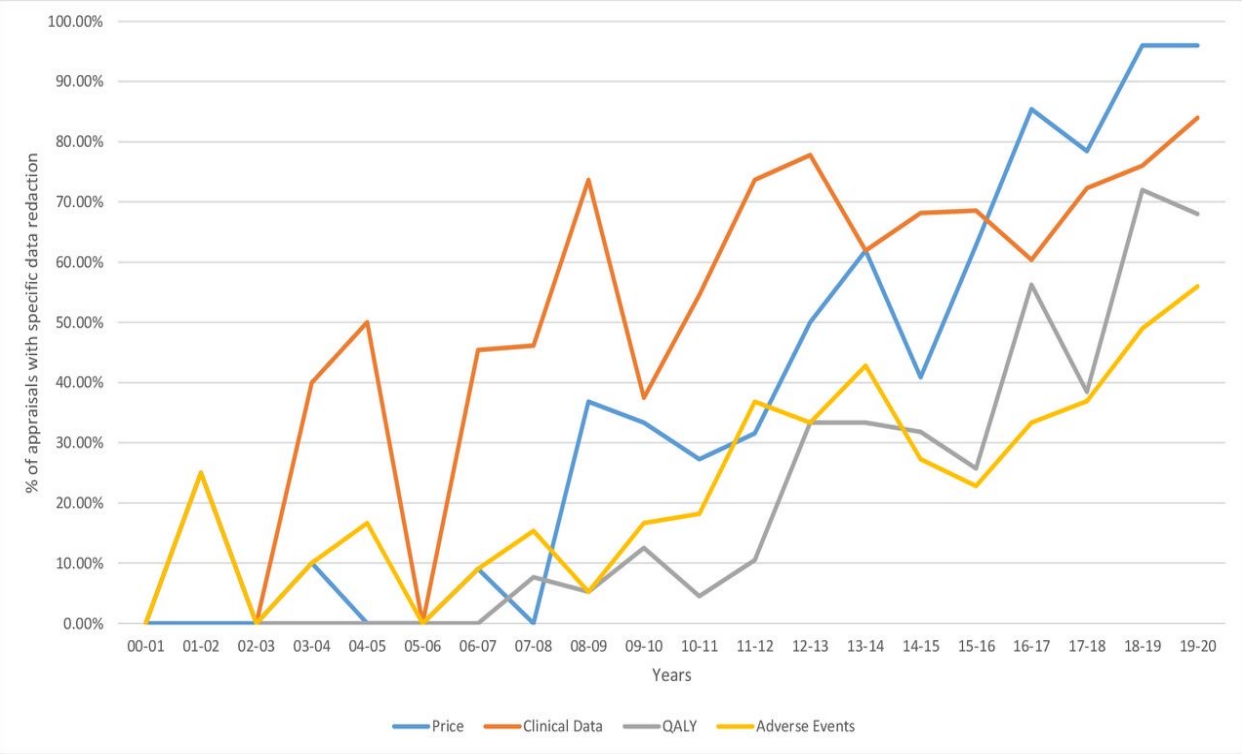
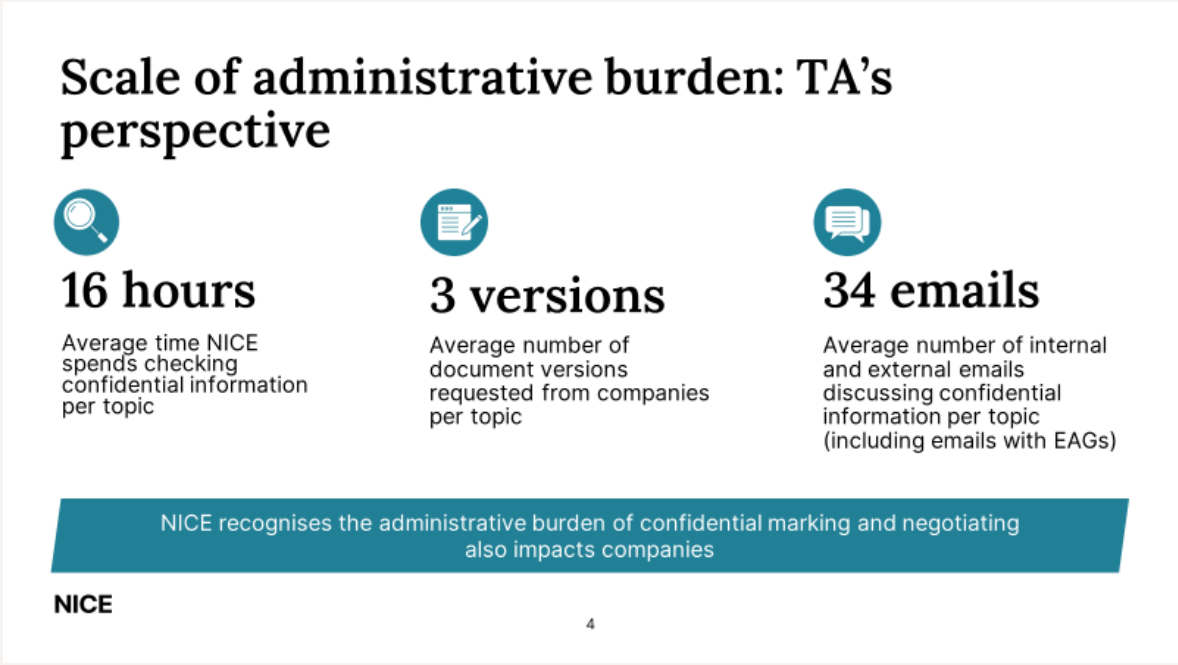


Figure 1. Redaction of data over time in NICE technology appraisals (n=408).[1]



Internal analyses – unpublished

AIC? ☺

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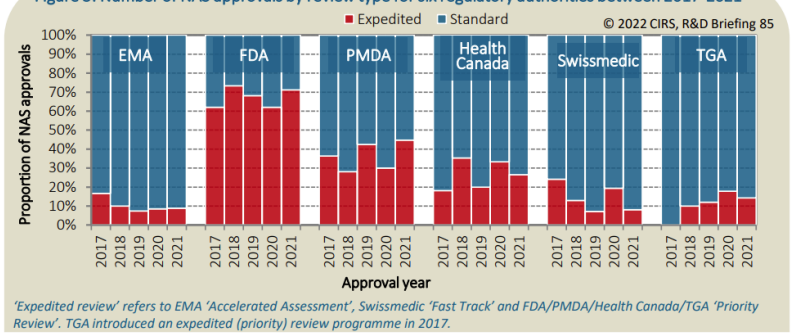
1. Osipenko L. Audit of data redaction practices in NICE technology appraisals from 1999 to 2019. BMJ Open 2021;11:e051812. doi: 10.1136/bmjopen-2021-051812

Also because …

We see ‘regulators’ speeding up their evaluations, using ‘expedited processes, accepting less mature data

Characteristics: Review type

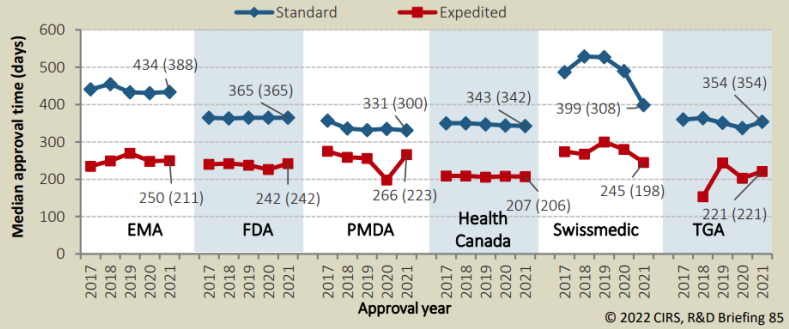
Figure 3: Number of NAS approvals by review type for six regulatory authorities between 2017-2021



‘Expedited review’ refers to EMA ‘Accelerated Assessment’, Swissmedic ‘Fast Track’ and FDA/PMDA/Health Canada/TGA ‘Priority Review’. TGA introduced an expedited (priority) review programme in 2017.

All six agencies offer an expedited process designed to hasten the review process of promising NASs (Fig. 3). In 2021, the ratio of expedited approvals to standard reviews was highest for FDA (71%), followed by PMDA (45%), Health Canada (26%), TGA (14%), EMA (9%) and Swissmedic (8%). TGA implemented its priority system in 2017; three expedited approvals were granted in 2018, another three in 2019, and five for each year in 2020 and 2021. The proportion of expedited approvals has been consistently high for FDA

Figure 4: NAS median approval time by review type for six regulatory authorities between 2017-2021



‘Expedited review’ refers to EMA ‘Accelerated Assessment’, Swissmedic ‘Fast Track’ and FDA/PMDA/Health Canada/TGA ‘Priority Review’. TGA introduced an expedited (priority) review programme in 2017. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time. N1 = overall approval time for 2021; (N2) = time from submission until the end of scientific assessment (see p.23) for 2021.

EMA was the agency with the greatest difference in median approval time between expedited and standard review in 2021, with a difference of 184 days, whereas the smallest difference was for PMDA, with 65 days. The difference between standard and expedited review was 154 days for Swissmedic, 136 for Health Canada, 133 for TGA and 123 for FDA. Interestingly, for Swissmedic, the additional label negotiation activities taking place following

Centre for Innovation in Regulatory Science (2022) R&D Briefing 85: New drug approvals in six major authorities 2012–2021: Focus on Facilitated Regulatory Pathways and internationalisation. Centre for Innovation in Regulatory Science (CIRS), London, UK.

We see greater use of ‘pre-print’, esp in context of COVID

news feature

Maria van Kerkhove, COVID-19 Technical Lead at the WHO, gives one of many press conferences . Credit: WHO

Rise of the preprint: how rapid data sharing during COVID-19 has changed science forever

Medical discoveries have been shared at an unprecedented pace during the COVID-19 pandemic, but so have fraudulent studies, which has led to worries about scientific integrity.

Clare Watson

Watson, C. Nature Mediicine. Vol 28.January 2022. 2-5. Rise of the preprint: how rapid data sharing during COVID-19 has changed science forever | Nature Medicine

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What is the problem we are trying to solve?

Increasing level of confidential information

Limited HTA capacity

Public demand for more transparency

The balancing act of transparency

Timely, useful, usable guidance

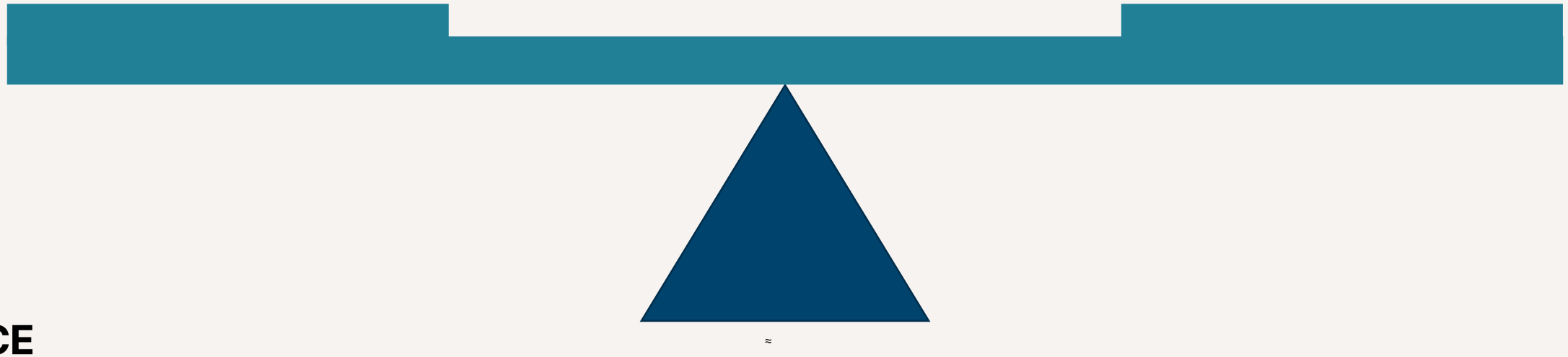
Academic publication

Industry interests

Public interest

User insight

Reduced resource burden



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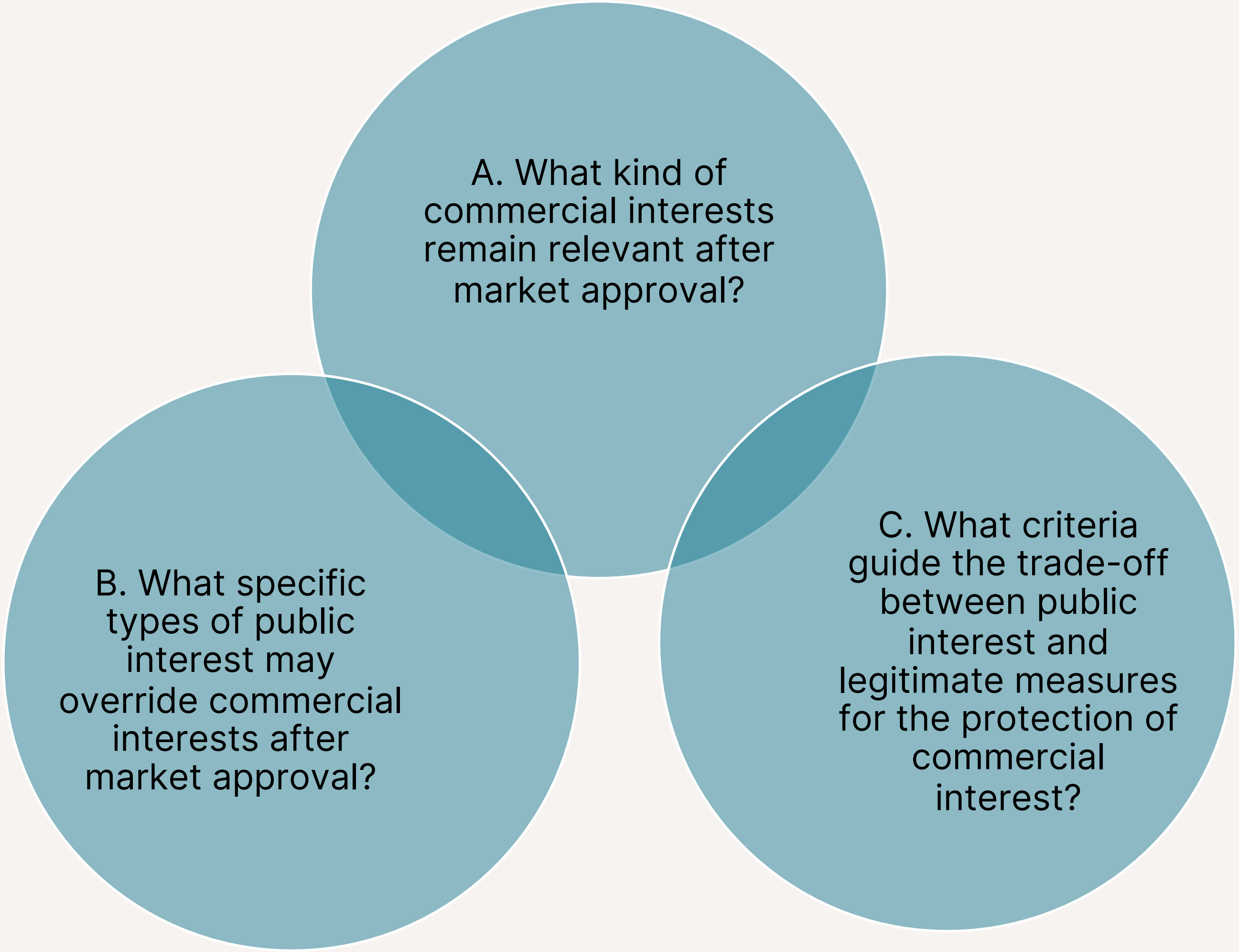
Weighing up 'public' with commercial interest …



[illegible]

1. Research participants
2. Clinical researchers
3. Research ethics committees and institutional boards
4. Clinical practice guideline development panels and health technology assessment institutions
5. Patients and their doctors
6. Public research sponsors
7. Health insurance companies

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Strech and Littmann. Lack of proportionality. Seven specifications of public interest that override post-approval commercial interests on limited access to clinical data. Trials 2012, 13:100.

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[Whose Job is it Anyway? Full Service - YouTube]

International collaboration

NICE National Institute for Health and Care Excellence

cadth Canada's Drug and Health Technology Agency

Health technology evaluations must strike a critical balance between ensuring transparency of the evidence and decision-making and protecting confidential information.

The three organisations operate in different health systems but share common aims and values. Given these similarities, NICE, CADTH and ICER have been working together with the aim to create a more consistent approach to how our agencies handle clinical data. We have published a joint statement setting out the changes.

ICER INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

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Position Statement (April 2023)

8. For evaluations starting after April 2023, NICE technology appraisals and CADTH will no longer routinely redact clinical data that is awaiting publication when we publish our guidance. ICER will allow redaction of data that is formally planned for public release for 12 months, as academic in confidence.

9. For other clinical data, we have defined a list of categories for which we expect the data to be made available in the public domain where it informs the development of our guidance (see appendix A). We will review and update the list as new challenges arise.

10. Respecting the different contexts in which our agencies operate we will have our own policies for managing clinical data for which there is no plan to publish.

11. We will continue to accept redaction of data that is commercially sensitive, such as information around pricing and terms of reimbursement arrangements.

12. We consider it the responsibility of the evidence holder to ensure they respect the principle of transparency, especially when it concerns clinical data that has been sourced directly from people using healthcare services.

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Recognising the different policy contexts we operate in …

- 'Public interest test' in the context of 'status' of recommendations (i.e. reimbursement advice / funding requirement (CADH & NICE, resp).
- 'Relationship' with life sciences industry: e.g. process and methods development at NICE in context of 'voluntary scheme for pricing and access', for example.

Clinical data not yet in the public domain but either: • awaiting publication, including in a journal or • will be released into the public domain by regulatory authorities	No	To avoid redaction of data that will subsequently be available and when publishing in committee papers will not jeopardise publication elsewhere. The International Committee of Medical Journal Editors (ICMJE) recommendations on overlapping publications state that it 'does not consider results or data contained in assessment reports published by health technology assessment agencies, medical regulators, medical device regulators, or other regulatory agencies to be duplicate publication'.
Clinical data that has not been made publicly available and for which there is no plan for the data to become publicly available	Yes, except for minimum reporting requirements. Data collected within NHS clinical practice as part of a managed access agreement cannot be considered confidential unless it meets other criteria, for example it allows for subject identification.	In recognition that there will be unpublished clinical data that will be confidential. However, to allow transparent reporting of decision making, NICE has outlined minimum reporting requirements for data which is likely to be fundamental to committee decision making (see table 3.1). Clinical data should be treated as clinical data without a publication plan if: • there is clinical data awaiting first public presentation at a congress that is scheduled to take place after documentation from NICE would be released to the public, and • this data is not awaiting publication in a journal or within marketing authorisation documentation.

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principles-for-marking-and-redacting-confidential-information.docx (live.com) – viewed 26/04/2023, 09:01

Further opportunities for collaboration …

(12) Joint work should be produced following the principle of good administrative practice, and it should aim to achieve the highest level of quality, transparency and independence.

(29) Transparency and public awareness of the process is essential. Where there is confidential data for commercial reasons, the reasons for confidentiality need to be clearly set out and justified and the confidential data well delimitated and protected.

(44) In order to ensure the inclusiveness and transparency of the joint work, the Coordination Group should engage and consult widely with stakeholder organisations with an interest in Union cooperation on HTA, including patient organisations, healthcare professional organisations, clinical and learned societies, health technology developer associations, consumer organisations and other relevant non-governmental organisations in the field of health. A stakeholder network should be set up to facilitate dialogue between stakeholder organisations and the Coordination Group.

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… and with regulators!

Activity	Expected outcomes	Actioned as part of EUnetHTA21 deliverables	Voluntary activity by individual HTA bodies
Exchange of information on the respective assessments of medicinal products by regulators and HTA bodies			
Foster opportunities for information exchange between regulatory assessors and HTA authors on identified products of mutual interest, including ATMPs	Proactive identification of relevant products that should be subject to discussion between regulators and HTAs. Arrange discussions between EMA and HTA bodies on ATMPs as suggested in the EC/EMAs action plan on ATMPs	X	
	Progress identification of PLEG requirements as a result of such product-specific discussions	X	
	Explore feasibility of earlier engagement between regulators and HTA bodies during the regulatory assessment, respecting remits. Assess feasibility and conduct a voluntary pilot for early engagement, evidence sharing, and managing uncertainties.	X	
	Initial drafting of rules for cooperation, in particular by exchange of information, with the European Medicines Agency on the preparation and update of joint clinical assessments of medicinal products	X	
Continuous optimisation of regulatory outputs as reference for down-stream decision making			
Further optimisation of the regulatory assessment report to facilitate uptake of regulatory consideration in the context of HTA	Regular experience reviews to update the assessment report guidance (e.g. feedback from product specific discussions), also to be complemented with information sessions / trainings		X
Continue sharing experience on labelling and EPARs information, e.g. regarding information on subpopulations	Share guidance on optimising information on subpopulations, e.g. in labelling and EPARs		X
Optimise the published information on orphan medicinal products	Obtain feedback from HTAs on the experience with the Orphan Medicines Assessment Report (OMAR) in order to continuously improve this output		X

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Take home messages

- Transparency is all our business.
- The road to ‘full transparency’ is long.
- Getting ‘there’ requires GRIT (‘guts’, ‘resilience’, ‘initiative’ and ‘tenacity’)
- Only by collaborating will we succeed.
- For patients and their families.

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Thank you.

Further interesting read: The HealthWatch Newsletter (healthsense-uk.org)