ECDC public consultation

'Draft EU guidelines on the prudent use of antimicrobials in human medicine'

Public consultation and received comments

In the context of ongoing work against the rising threats from antimicrobial resistance and given the role of antimicrobial misuse and overuse in the emergence and spread of resistance, the European Commission asked ECDC to develop draft EU guidelines on the prudent use of antimicrobials in human medicine, including generic principles of good practice on the appropriate use of antimicrobial agents in human medical practice in the EU. ECDC then produced a technical report with proposals for EU guidelines on the prudent use of antimicrobials in humans.

This report is a key contribution to support the European Commission in its aim to produce a finalised set of EU guidelines. As part of the process to develop the proposals and in order to receive comments from the scientific community and stakeholders, ECDC launched a public consultation, which closed on 5 September 2016. Comments were submitted by 48 organisations and 18 individuals.

This document presents the comments received from the public consultation in two sections: the first section includes all comments submitted on behalf of organisations, while the second one contains all comments submitted by individuals. All comments were taken into account in the revision of the draft, ensuring that the content was consistent with the purpose and scope of the request and in line with the principles for guideline development.

Details on how individual comments were taken into account can be made available upon request.

This collection of comments was gathered from a public consultation on a document originally released as an ECDC draft technical report:
European Centre for Disease Prevention and Control. Proposals for draft EU guidelines on the prudent use of antimicrobials in human medicine. Stockholm: ECDC; 2016.

In February 2017, after a careful review process, ECDC published the final technical report:
European Centre for Disease Prevention and Control. Proposals for EU guidelines on the prudent use of antimicrobials in humans. Stockholm: ECDC; 2017

Comments on behalf of organisations

Section of document	Comment and rationale – proposed change
Alere (United Kingdom)	
Scope	The outlined scope of the report states that it will not cover specific medical conditions, however various disease-specific considerations are provided throughout the draft guidance, such as recommendations around sepsis and respiratory tract infections. At present the scope of this guidance is not clear. Clarify the scope of the guidance in relation to specific medical conditions.
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment [17-23].' When used alongside signs, symptoms and history taking, rapid point of care diagnostics for defined patient groups can have a significantly positive impact in terms of optimising antimicrobial treatment. As evidence shows, tools such as C-Reactive Protein Point of Care Testing can support practitioners to prescribe antibiotics more effectively and therefore reduce the risk of increased levels of antimicrobial resistance. With this in mind, it would be useful to include a more comprehensive source of references that support this crucial intervention. Insert additional references for this recommendation, including: • Andreeva E, Melbye H. Usefulness of C-reactive protein testing in acute cough/respiratory tract infection: an open cluster-randomized clinical trial with C-reactive protein testing in the intervention group. BMC Family Practice2014. 15:80 • DOI: 10.1186/1471-2296-15-80 • Hunter R. Cost-effectiveness of point of-care C-reactive protein tests for respiratory tract infection in primary care in England. Adv Ther. 2015;32(1):69-85. • Hopstaken R, Verdijk N, Van den Broek N, et al. [CRP-sneltest in de dagelijkse praktijk]. Huisarts Wet. 2012;55(9):388-392. It would also be useful to highlight the important role that rapid point of care diagnostics can have in supporting antimicrobial prescribing decisions in not just healthcare facilities, but also within a community setting, for example in conjunction with local pathology services. This has been supported by official guidance from the Department of Health, which states: 'The possibility of bringing these tests [rapid point of care diagnostics] into the community has the potential to radically improve diagnostic certainty in primary care.' * *Pinder R, Sallis A, Berry D, Chadborn T. Behaviour change and antibiotic prescribing in healthcare settings: Literature review and behavioural analysis (2015) Available at: www.gov.uk/government/publications/antibioticprescribing-and-behaviour-change-inhealthcare-settings Clarify that rapid point of care diagnostics can also support improved antimicrobial prescribing decisions within community settings.
Prescribers	In line with the outlined scope of this guidance and the inclusion of 'good clinical practice', it would be useful to make reference to examples of exemplary clinical practice such as the TARGET Antibiotics Toolkit, produced jointly by the Royal College of General Practitioners and Public Health England, and includes a wide variety of important resources for commissioners, practitioners and patients. The resources promote key aspects of an effective antimicrobial stewardship programme, including the use of rapid point of care diagnostics, such as C-Reactive Protein Point of Care Testing. Make reference to examples of good clinical practice, such as the TARGET Antibiotics Toolkit.
Diagnostic industry	Whilst the guidelines recognise the role of the pharmaceutical industry in efforts to ensure the prudent use of antimicrobials, the failure to similarly include the role of the diagnostic industry represents a major omission. As is highlighted within the guidance, rapid point of care diagnostics can have an important role in optimising antimicrobial treatment and reducing the threat of antimicrobial resistance. There is also a significant body of evidence demonstrating the beneficial impact that diagnostics can have in supporting healthcare practitioners to reduce inappropriate antimicrobial prescribing and encourage improved antimicrobial stewardship. With this in mind, the guidelines would benefit from incorporating a specific segment on the role of the diagnostic industry, drawing upon relevant areas of guideline (for instance the British In Vitro Diagnostics Association's Code of Conduct) Include a new segment (13) on the key role of the diagnostic industry.
ATB-Raisin network (France)	
	Please see also comments by Dumartin Catherine (France); Lieutier-Colas Florence (France); Elias Christelle (France)
International-organisations, agencies	'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns to support appropriate antimicrobial use [expert consensus].' International collaboration could address organisation to prevent cross-border spread Add : 'international collaboration in designing and implementing process to prevent cross-border threats'
National and regional	The list of items is quite long and items could be grouped by categories, for instance all items related to clinical guidance Group item e, f, g and i under a title 'national clinical guidance' Group h and q
Healthcare facilities	'Guidelines for the diagnosis and management of infections. Example of indicator: proportion of prescriptions compliant with guidelines' Guidelines on management of infections could include information on infection control Add: '…management of infections, including prevention of cross transmission when relevant'.
Healthcare facilities	'An audit of perioperative antimicrobial prophylaxis choice, timing and duration'. Root-cause analysis of treatment failure/non-compliance to guidelines could be an interesting quality indicator Add: '…duration, and root-cause analysis of adverse events related to antimicrobial use (e.g. treatment failure…)
Infection control practitioners	The specific role of compliance to infection control guidelines to reduce the need for antimicrobial treatments could be recalled Add: 'Ensure compliance with guidelines for infection prevention and control, including vaccination, to reduce the need for antimicrobial use.'
Public/patients	Public should also be informed on how to prevent cross transmission when they carry a resistant bacteria. Add: Get informed on how to prevent cross-transmission when you are carrying a resistant micro-organism' The French national action plan Propias (see below could be cited as references for these items)

Section of document	Comment and rationale – proposed change
Reference	The French national action plan for healthcare-associated infections prevention could be mentioned as it includes an major part on antimicrobial resistance prevention and control and sets targets for improvement of prescribing (e.g. proportion of surgical prophylaxis > 24 h under 10% and proportion of antibiotic treatment lasting > 7 days without justification < 10%) « Ministère des affaires sociales, de la santé et des droits des femmes. Instruction du 15 juin 2015 relative au programme national d'actions de prévention des infections associées aux soins (Propias) 2015 »
bioMérieux (France)	
Definitions	'Antimicrobial stewardship programmes refer to coordinated programmes that implement interventions to ensure appropriate antimicrobial prescribing and effective antimicrobial treatment, in order to limit antimicrobial resistance and to prevent Clostridium difficile infections.' Suggestion to slightly enlarge the definition of Antimicrobial stewardship programmes Antimicrobial stewardship programmes refer to coordinated programmes that implement interventions to ensure appropriate antimicrobial prescribing and effective antimicrobial treatment, in order to limit antimicrobial resistance, enhance patient health outcomes and to decrease unnecessary costs.
International	'Ensure access to essential antimicrobials by supporting market availability [expert consensus].' There is a crucial need to support R&D and access to diagnostic tools in order to control AMR Modify: Ensure patient access to essential antimicrobials and diagnostics by supporting their development and market availability [expert consensus]
International	'Develop European evidence-based guidelines on the use of rapid and point-of-care diagnostics [expert consensus].' The development of European guidelines is important, but the uptake at Member State level has to be facilitated Modify: Develop European evidence-based guidelines on the use of rapid and point-of-care diagnostics and facilitate their implementation at Member State level [expert consensus]
National and regional - governments	'Explore incentive systems for appropriate prescribing [expert consensus] [9]. Appropriate prescribing is only possible if appropriate diagnostic tests are used. The current low cost of antimicrobials versus the much higher cost of the new rapid molecular diagnostics makes their uptake difficult. Unfortunately, the societal value attributed to these rapid diagnostic tests to support the development and responsible use of antibiotics is not considered in setting the reimbursement price. Modify: Explore incentive systems for appropriate prescribing [expert consensus] and use of appropriate diagnostic technologies to improve the prescription of ATB treatment
Healthcare facilities	Surveillance of antimicrobial resistance patterns at all levels – national, local, hospital and ward level - is essential to set up antimicrobial policies. Knowledge of bacterial ecology is increasingly playing an important role in better controlling the emergence of resistant bacteria. Add: Contribute to hospital-wide, national and regional surveillance studies and prevalence surveys, including molecular epidemiological investigations.
Healthcare facilities	Transmission drives resistance. Screening patients and healthcare workers for multidrug-resistant organisms (MDRO) is a key measure to contain the spread of resistance. Add: 'Screen patients and healthcare workers for multidrug-resistant organisms'
Laboratories	Need to incentivize use of new diagnostic technologies Add: Encourage the use of new diagnostic technologies to fasten time to results (such as PCR tests)
Prescribers	In the community, often no test to differentiate between viral or bacterial infection for example, is done before antibiotic prescription. Add: Encourage the use of rapid diagnostic tests to prescribe antibiotics only when necessary
Prescribers	Appropriate prescribing is only possible if appropriate diagnostic tests are used. The current low cost of antimicrobials versus the much higher cost of the new rapid molecular diagnostics makes their uptake difficult. Unfortunately, the societal value attributed to these rapid diagnostic tests to support the development and responsible use of antibiotics is not considered in setting the reimbursement price. Add: Encourage the use of diagnostic tests to improve the prescription of antibiotic treatment and adaptation of antibiotic therapy (both biomarkers and microbiological tests including PCR)
Research	'Promote research on rapid and point-of-care diagnostics to support evidence-based guidelines for the role of diagnostics in appropriate antimicrobial prescribing [expert consensus].' It is not only necessary to fund and promote research on rapid and point-of-care diagnostics, but also to ensure their uptake and patient access. Research showing the value of these diagnostic technologies needs also to be encouraged. Modify: Promote and fund research on the development and uptake of rapid and point-of-care diagnostics to support evidence-based guidelines for the role of diagnostics in appropriate antimicrobial prescribing [expert consensus]
Diagnostic industry	Suggestion to add a chapter on the diagnostic industry In vitro diagnostic companies play a key role as they highly contribute to: - Antibiotic stewardship (antibiotics only when necessary in primary care, disease use of board spectrum antibiotics in hospitals) - Resistance monitoring - Resistance transmission prevention by multi-drug resistant organisms (MDRO) - More efficient patient recruitment in new antibiotic trials Their use should be encouraged and the development of new diagnostic tools should be supported.
British Dental Association (United Kingdom)	
General comment	As a proponent of the dental profession's role in addressing AMR, the BDA largely supports these guidelines and welcomes the expert consensus approach to their development.

Section of document	Comment and rationale – proposed change
Prescribers	'dentists should prescribe antimicrobials according to guidelines. Antimicrobials should not be used as a substitute to dental operative intervention [40-42].' We support the statement as it stands, but would note that situations might arise in which a dentist may feel justified in prescribing outside the national guidelines – which are not legislative standards. A dentist prescribing outside the guidelines, with fully informed and valid consent from the patient, must properly record and justify the decision. 1. Modify: ….dentists should aim to prescribe antimicrobials according to guidelines. Where the dentist feels it appropriate to prescribe, or not to prescribe, outside the guidelines, valid consent should be sought from the patient and reasons for the decision fully documented and justified. The BDA supports this principle and believes that it should be explicitly extended to other healthcare professionals, who also prescribe antimicrobials for dental pain. We note that general medical practitioners in England and Wales see approximately 600, 000 patients per year for dental problems. As they lack the specialised training and equipment to carry out the appropriate treatment, they have a greater tendency than dentists to prescribe antibiotics as a substitute. 2. Modify: Antimicrobials should not be used by dentists or other healthcare professionals as a substitute to dental operative intervention.
Prescribers	Both education of the public and proper funding of public dental services are central to addressing this issue. Dental contracts must be designed and funded to support dentists in providing time-consuming operative interventions, particularly in unscheduled care, rather than incentivising the prescribing of antibiotics. Add to Section 2: *Ensure that proper funding policies are established for the provision of dental unscheduled clinical interventions for the management of dental infections.*
Education/academics	'Require participation in a minimum number of certified education activities on antimicrobial prescribing and use' Clinicians would be expected to plan their training and education in the light of regular review of their learning needs. All postgraduate clinicians should work to a Personal Development Plan that should be strategic, dynamic and responsive, directing the timing and required number of all education and training activities. The key issue is that learning opportunities in relation to antimicrobial prescribing must be readily accessible, high quality, relevant and frequently presented. Modify*: …recommend participation in a minimum number of certified education activities on antimicrobial prescribing and use ensuring that such opportunities are high quality, relevant, readily accessible and frequently presented.*
British In Vitro Diagnostics Association (BIVDA) (United Kingdom)	
	Please see also comments by Alere (United Kingdom)
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment' BIVDA would also support the strengthening of this line to reflect the recommendation in the final report of the O'Neill Review into AMR that states: 'Rich countries must lead the way to change this: they should make it mandatory that by 2020 the prescription of antibiotics will need to be informed by data and testing technology wherever available and effective in informing the doctor's judgement to prescribe'.* * O'Neill, J. Tackling Drug-Resistant Infections Globally: Final Report And Recommendations The Review On Antimicrobial Resistance (2016) Strengthen the sentence to say that rapid and/or point-of-care diagnostics, where possible, should be used to complement clinical assessment and optimise antimicrobial treatment.
British Medical Association (United Kingdom)	
International	There is a great urgency for investment in the surveillance of resistant infections, and international cooperation for data-sharing procedures to better our global response capacity. To enhance the global surveillance system, we further recommend international collaboration and investment into supporting and building laboratory capacity in low-middle-income countries that have been severely affected by microbial resistance.
Prescribers	Ensuring adequate microbiology services and improved diagnostics – the diagnosis of infection is essential for informing doctors' decision-making when prescribing antimicrobials. Mechanisms that facilitate accurate and timely diagnosis of infection are key to improving antimicrobial prescribing in primary and secondary care. This includes providing adequate resources for effective microbiology services and diagnostic tests, as well as developing better diagnostics where required.
Prescribers	Supporting family medicine/ general practice – the majority of antimicrobial prescribing in the UK occurs in general practice. While efforts are being made across primary care – including through medicines management teams – to improve antimicrobial prescribing, it is important to consider the environment in which antimicrobials are being prescribed. There is a need to ensure adequate investment and resources are provided to properly support GPs when prescribing antimicrobials. Consultation times need to be sufficient to allow GPs to properly assess patients, and if necessary to give explanations as to why antimicrobials have not been prescribed. Better access to timely diagnostic tests in primary care is also required to improve antimicrobial prescribing. The fragmentation of primary care – whereby services are delivered by numerous providers – risks undermining efforts made by GPs to reduce antimicrobial prescribing. Reducing this fragmentation and preserving list-based general practice would help ensure improvements in antimicrobial prescribing by maintaining continuity, trust and consistency.
Healthcare facilities	Greater accountability for antimicrobial stewardship in hospitals – it is often unclear in hospitals which staff have 'ownership' of antimicrobial prescribing and responsibility for minimising resistance. Effective local leadership is a key factor in improving the quality of antimicrobial prescribing. There is a need to identify clinical infection specialists who can 'champion' appropriate antimicrobial prescribing locally, and take ownership of antimicrobial resistance. These 'antimicrobial champions 'would ensure that all hospital doctors had access to support when prescribing antimicrobials, and help ensure that best-practice guidance on antimicrobial prescribing is followed.
Center for Disease Control and prevention (USA)	
Prescribers	'if antimicrobial treatment is not considered necessary, give patients advice about the expected natural history of the illness, the limited or absent benefit of antimicrobial treatment, and the potential unwanted side-effects of antimicrobials such as diarrhoea and rash, as well as advice about actions in case of worsening clinical condition (safety netting)'. This bullet addresses communications with patients about not prescribing antibiotics when they are not indicated. This is a very nice list of points that prescribers should address. Did you all consider also including in this list provide recommendations for symptom management? A US study demonstrated that parents who received messages that their child did not need antibiotics in combination with messages about how to manage their child's symptoms were more satisfied with the visits (Mangione-Smith, R., et al. (2015). 'Communication practices and antibiotic use for acute respiratory tract infections in children.' Annals of Family Medicine 13(3): 221-227.) We have tried to incorporate recommendations for symptom management in our messages to US prescribers about appropriate outpatient antibiotic prescribing.

Section of document	Comment and rationale – proposed change
Prescribers	'consider delayed antimicrobial prescribing with appropriate safety netting for adults or children in specific circumstances and according to guidelines [36-38]. Example: delayed antimicrobial prescribing for upper respiratory tract infections' This bullet addresses delayed antimicrobial prescribing. Why is upper respiratory tract infections highlighted as the example for delayed prescribing? I wonder, if without more explanation, this example might inadvertently convey the message that upper respiratory tract infections may sometimes need antibiotic therapy. Is this example meant to address acute rhinosinusitis? The US guidelines use different terminology for viral upper respiratory tract infections (URIs) and acute bacterial rhinosinusitis, which is useful in communicating about when antibiotics are and are not needed.
Council of European Dentists (Belgium)	
General comment	The CED welcomes the expert consensus approach to the development of the draft EU Guidelines and in the large majority supports the general approach and the recommendations presented in each section. In particular, CED considers that it is, indeed, timely and appropriate to provide guidance on generic elements of good practice. The CED General Meeting has for some time unanimously agreed a resolution that supports best practice in prescribing and emphasises the responsibility of the dental profession in contributing to the reduction of AMR.
	Please see comments by the British Dental Association (United Kingdom)
Croatian Society of Clinical Microbiology of the Croatian Medical Association (Croatia)	
Healthcare facilities	In some countries clinical microbiologists are consulting on antimicrobial therapy and are taking active part in AMS programs. Even in countries where microbiology is more laboratory based it is of great benefit to stimulate microbiologists to be more involved in clinical work and consulting – this is in line with the UEMS curriculum for medical microbiology. Defining CM as an essential member of an ASM team would further promote and strengthen clinical role of a medical microbiologist especially in countries where this role is still not well defined We think that a clinical microbiologist should be added as an essential member of the ASM team
Directorate General for Heath, Ministry of Health (France)	
Introduction	We strongly support emphasising that antimicrobials are unique among therapeutic medicines, and would further insist on this point. Add in introduction: 'Thus, antimicrobials require special attention and specific measures promoting prudent use at the national and international levels'
Introduction	Would add a sentence/short paragraph to emphasize that antimicrobial stewardship and good infection control practices are both necessary and complementary to reach the objective of controlling AMR. 'It should be emphasized that the ultimate goal of controlling AMR can only be reached with both strong infection control organisation and practices and prudent use of antimicrobials. Thus these guidelines should be viewed as complementary to infection control guidelines.'
Definitions	Possibly useful to remind the reader on the definition of multi-drug resistant microorganisms, by making reference to the consensus document published in 2012 'A multi-drug resistant bacteria is not susceptible to at least 3 classes of antibiotics to which the bacteria is normally susceptible'. Some microorganisms may fall into this category based on a unique resistance marker (eg., MRSA, VRE, ESBL).
Definitions	The addition of C.difficile infection (CDI) as a marker of Antimicrobial stewardship programme activities is questionable. Certainly, CDI is a marker of antibiotic overuse; however, there are numerous risk factors for CDI, community-based carriage, and it is unclear that ASP can reduce effectively CDI rates. In addition, CDI can be viewed as one marker among others, such as Candida or MDR superinfection. Suggest replacing the end of this sentence with: '…, in order to limit antimicrobial resistance and bacterial superinfection caused by multi-drug resistant microorganisms, or other microorganisms such as Candida or *C. difficile*'.
International	'Establish a new European platform for sharing best practice interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes [expert consensus]. Could the panel be more specific about the 'new European platform' and which 'relevant qualitative and quantitative outcomes' are targeted? Please describe in a few words how this platform is implemented and run. In addition, this task may be prepared within the upcoming AMR&HCAI JA, and then handed over to ECDC.
International	'Ensure access to essential antimicrobials by supporting market availability' requires that those essential drugs are first defined. Does the panel refer to the WHO list of essential drugs? Add a definition for 'essential antimicrobials' or refer to an existing list, or first state that this list needs to be established, and by which organisation (eg, EMA?).
International	'Development of European and national standards' needs stronger wording and addition of international harmonisation of interpretative susceptibility criteria. Replace: 'Encourage the development of European standards and adoption at the national level of standards..' Add: 'Encourage harmonisation of testing methods and interpretative criteria'
International	Perhaps a mention of the need for organisations and agencies to support and fund research into new antibiotics and alternative approaches would be in order, as this is important for good antimicrobial prescribing and stewardship (eg, alternatives, new rapid diagnostic tests, vaccines,..) Add a recommendation in support of funding of research into antimicrobial stewardship organisation and activities, behavioural sciences, and research and development of new drugs, alternatives, vaccines and diagnostic tests.
National -regional	'Integrate national antimicrobial stewardship activities into the national antimicrobial resistance plans that include infection prevention and control and vaccination, in a 'One Health' approach [expert consensus].' In the context of this sentence, mention of the 'One Health' approach seems to refer to infection control activities and vaccination, whereas One Health refers to transectoral activities Reword as : 'Integrate national antimicrobial stewardship activities, <u>together with</u> infection prevention and control and vaccination, within the national antimicrobial resistance plans developed according to <u>the transectoral</u> 'One Health' approach.'

Section of document	Comment and rationale – proposed change
National -regional	'Establish a national committee/ platform for the development, implementation and monitoring of clinical guidance for infection' is unclear: what is meant by clinical guidance for infection? Is this committee/platform issuing national guidelines for management of infection? How does this body 'implements' these? (it is unlikely that a committee can implement guidelines, although it can monitor their implementation). Add the word 'management' after 'clinical guidance for' (if as meant). Please specify more clearly the nature and role of this committee/platform, and from what type of body it could evolve (Scientific society, heath quality agency,..). Q: How does this recommendation differ from the following item?
National -regional	'Ensure national clinical guidance is reviewed and revised when there is a significant change in antimicrobial resistance, new evidence on management of infections or at regular intervals (e.g. 2–3 years) [expert consensus]. It may be unnecessary to revise guidelines routinely at 2-3 years in the absence of change in resistance patterns, or new evidence, as this may impose a unnecessarily high burden on the organisation producing guidelines. Suggest rewording as : '.. revised when there is a significant change in antimicrobial resistance, new evidence on management of infections, or at least every 5 years'
National -regional	Guidelines are already covered by the preceding bullet points
Healthcare facilities	'For hospitals': is this paragraph meant to cover all types of institutions (ie, acute care, long-term rehabilitation units, long-term acute care)? Could the panel make recommendations adapted to different types of activities?
Healthcare facilities	'The availability of facility-specific cumulative susceptibility reports for common bacterial pathogens against antibiotics that are recommended in the guidelines' Suggest also adding 'and activity-specific', e.g, for medicine, surgery, intensive care, rehabilitation and long-term care
Healthcare facilities	'Monitoring of quality indicators and quantity metrics of antimicrobial use with feedback to prescribers and prescriber actions agreed' Suggest rewording.
Healthcare facilities	'Establish a multi-faceted approach that may include elements such as clinic-based education, patient information leaflets [25] and public patient education campaigns combined with clinician training [21] in communication skills.' This recommendation would better fit within chapter 2 (national-regional level) or 5 (prescribers), rather than at the HCF level
Laboratories	'Provide facility-specific cumulative susceptibility reports for common bacterial pathogens against antibiotics that are recommended in the guidelines [expert consensus].' Susceptibility reports at the facility level may be misleading, depending of activities housed in the institution. Suggest providing facility and activity-specific levels for susceptibility reports
Laboratories	Emphasize the importance of making rapid diagnostic tests available for clinicians to help them decide on the indication or selection of antibiotics Add mention of evaluation and promotion of effective and reliable rapid diagnostic tests
Prescribers	'avoid antimicrobial treatment when there is evidence of viral infection or of a self-limiting bacterial infection [expert consensus]' and 'do not prescribe antibacterials for viral or self-limiting bacterial infections [34]. Example of indicator: Seasonal variation of the total antibiotic consumption (ATC code: J01) (in the community) [30,35]' Suggestion: it is a repetition, merge them
Prescribers	'avoid treatment for colonisation without evidence of infection [29] [expert consensus]' Treatment of colonisation can be justified to prevent infection, but usually not with antibiotics. Change wording as: 'Avoid antibiotic treatment for colonisation..'
Prescribers	'inform the patient about their antimicrobial treatment' Information of the patient: dialogue about an infectious problem may be a good opportunity for promoting preventive measures, such as immunisation. Suggest adding this point Add, at the end of the sentence: 'and on preventive measures to avoid relapses or reinfection'.
Infection control practitioners	The ICT can actively participate to limiting antibiotic use by promoting infection prevention and immunisation Suggest adding a sentence to mention the role of the ICT in preventing infection and unnecessary antibiotic use through promoting vaccination of at-risk patients and personnel (eg, for influenza).
Dutch Society for Medical Microbiology (The Netherlands)	
Healthcare facilities	'An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv).' To truly establish a sensible antibiotic policy, including empical therapies based on local epidemiology, the microbiological laboratory should be part of the antimicrobial stewardship team. In many countries these specialists are in fact leading the stewardship teams already. Change to: An antimicrobial stewardship team including at least a clinician (iii), a clinical microbiologist (iv) and a pharmacist (v). 1. Add amongst the recommendations the description of such a specialist: A microbiologist with expertise in (consultation of) infection management.'A clinician with expertise in the management of infections to be responsible for the antimicrobial stewardship team.' In many hospitals the stewardship team is in fact led by a physician specialized in clinical microbiology. Change (shorten) 3biii to: 'A clinician with expertise in the management of infections.' 2 Add amongst the recommendations in 3b: A physician who is professionally involved in the diagnostics, prevention and treatment of infectious diseases should be responsible for the antimicrobial stewardship team.

Section of document	Comment and rationale – proposed change
Laboratories	The role and responsibility of the clinical microbiologist is not documented in this draft proposal. Laboratories don't 'do' anything, it is the people working in laboratories who carry responsibilities and follow guidelines. Change title to: Clinical microbiologists and microbiological laboratories 1. Change text to: Clinical microbiologists play a key role in providing diagnostic information and the expertise required to exercise effective infection control, prevention of antimicrobial resistance and adequate treatment of infection. Furthermore, they provide advice and guidelines on optimal diagnostic strategies for infections. Current evidence and expert opinion support the following as effective elements of guidelines to be followed by clinical microbiologists and to be implemented at the laboratory level: 2. Add the following responsibilities: d. be available to clinicians for counselling on difficult to treat pathogens, complicated infectious diseases and diagnostics of infectious diseases. e. communicate indications of nosocomial or community outbreaks to the relevant hospital commissions and/or authorities, and, where applicable, actively assist in the management of such outbreaks.
EPSA – European Pharmaceutical Students' Association	
National and regional	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8].' In order for national public health campaigns to reach the target public maximally, collaboration with both professional and student healthcare organizations can be highly beneficial as they have the human resources and knowledge that are necessary. Add: '... national campaigns, in collaboration with both professional and student healthcare organisations, …'
National and regional	'Promote the introduction of electronic antimicrobial prescribing systems able to link clinical indication, microbiological and consumption data [expert consensus].' In some EU countries, pharmacists do not have a link to clinical indications on prescriptions, so when disposing they are not really able to do a medication check. This recommendation is therefore very important to overcome this limitation.
Prescribers	Prescribing and selling of antibiotics at the same time should not be allowed (Birna Trap, Ebba Holme Hansen, Hans V Hogerzeil. Prescription habits of dispensing and non-dispensing doctors in Zimbabwe. Health Policy and Planning. 2002;17(3):188-295.http://heapol.oxfordjournals.org/content/17/3/288.full.pdf+html) The reason for this is that it can generate economic arguments for doctors to prescribe antibiotics, which can result in a lower quality of healthcare Add new point: 'Doctors should not be allowed to both prescribe and sell/dispense antibiotics at the same time.'
Pharmacists	Pharmacists can help reducing inappropriate use of antibiotics as self-medication with appropriate counselling when dispensing, so that in countries where it is legally allowed to dispense some antibiotics as self-medication, they will only be dispensed when a trained medication specialist would approve. Add: 'Ensure responsible dispensing and use of antibiotics self-medication through appropriate counselling.'
Pharmacists	'Ensure that the patient understands the dosage and duration of treatment and promote returning leftover antimicrobials to the pharmacy [expert consensus].' Patient adherence should be stressed, as explaining the dosage and duration of the treatment is not the same as encouraging adherence to the therapy. Add: Ensure patient's compliance by explaining the nature of the disease, presenting the change in symptomatology using common vocabulary, focusing on requirements for efficiency and consequences of non-adherence.
Education/academics	'Ensure that all healthcare professionals are regularly trained on appropriate antimicrobial use [14,46]. Example: require participation in a minimum number of certified education activities on antimicrobial prescribing and use' Very important point and something that can be included in the continuous professional development programmes for healthcare professionals.
Education/academics	'Include training on prudent antimicrobial use in medical, nursing, pharmacy, dentistry and midwifery schools [expert consensus] [14,20]' This training should be given, at least partially, through interprofessional education with different groups of healthcare students. EPSA, EMSA and EPSA have already acknowledged the importance of interprofessional collaboration on fighting antimicrobial resistance, which starts by sufficient interprofessional education (http://www.epsa-online.org/images/EDSA_EMSA_EPSA_Policy_paper_on_the_spread_of_antimicrobial_resistance.pdf). As fighting antimicrobial resistance is a challenge for a broad range of healthcare professionals, interprofessional education can be a very important tool to ensure immediate interprofessional collaboration on this topic under young healthcare professionals. Add: '... midwifery schools. This training should be accompanied by a strong practical component in interaction with other healthcare students, academics and public health authorities.
Public/Patients	Prevention of antimicrobial resistance starts in the first place by preventing the occurrence of infections that are caused by easy avoidable causes such as lack of basic hygiene precautions. Next to education in primary and secondary school as mentioned before, there is also a need for further education of adults about prevention measures such as hygiene and vaccination. Add: 'Get informed about appropriate infection prevention, antimicrobial use, antimicrobial resistance and adverse reactions to antimicrobials [expert consensus]'
11. Research	Research on vaccines should be encouraged and supported, as this preventive measure has an important impact on reducing the spread of antimicrobial resistance (http://www.vaccineseurope.eu/wp-content/uploads/2013/09/AMR-and-Vaccines-June-2013.pdf). Add: Promote research on vaccination.
ESCMID Study group for antibiotic policies (ESGAP)	
National and regional	'A clinician with expertise in the management of infections to be responsible for the antimicrobial stewardship team.' And 'Salary support and dedicated time for antimicrobial stewardship activities.' The compliance with the recommendations is not feasible if there are not enough specially trained physicians and other professionals. Add: ensure appropriate number of experts in the field of antimicrobial stewardship through education of sufficient number of infectious disease specialists and other professionals
Education/academics	'Ensure that all healthcare professionals are regularly trained on appropriate antimicrobial use [14,46]. Example: require participation in a minimum number of certified education activities on antimicrobial prescribing and use' The recommendations for the prescriber level are not feasible without proper education of physicians in all stages Add: ensure that antimicrobial stewardship is included in the specialty training curricula for all clinical specialties
EUROCAM (Complementary and Alternative Medicine) (Belgium)	

Section of document	Comment and rationale – proposed change
Prescribers	Unless antibiotics are strictly necessary, prescribers could consider the use of certain CAM (Complementary and Alternative Medicine) treatments in mild to moderate infectious illness where there is evidence for effectiveness e.g. in respiratory and urinary tract infections. Research data can be found in the EUROCAM paper 'The role of Complementary and Alternative Medicine (CAM) in reducing the problem of antimicrobial resistance' Add: 'consider the use of certain CAM (Complementary and Alternative Medicine) treatments in mild to moderate infectious illness where there is evidence for effectiveness e.g. in respiratory and urinary tract infections. [http://www.cam-europe.eu/dms/files/Position_Papers/EUROCAM_PositionPaper_CAM_and_AMR_November2015.pdf] Add the reference suggested: The role of Complementary and Alternative Medicine (CAM) in reducing the problem of antimicrobial resistance, 2015.
European Association of Hospital Pharmacists (EAHP) (Belgium)	
Introduction	'Combined with the meagre development of novel antimicrobials, the spread of resistance to existing ones is leading to loss of effective options for the treatment and prevention of infections, representing a health security threat for Europe' The global nature of the problem should not be under-represented. The global importance and example of these guidelines should not be underestimated either. Modify: 'security threat for Europe and the world.'
Definitions	The guidelines should have the ambition of giving clarity to EU member states on which healthcare professionals should be involved in, and responsible for, implementation of antimicrobial stewardship programmes. Add new definition: antimicrobial stewardship team. An antimicrobial stewardship team is the group of healthcare professionals responsible for implementation of an antimicrobial stewardship programme. Core members of a multidisciplinary antimicrobial stewardship team include an infectious diseases physician and a hospital pharmacist with infectious diseases training, with the inclusion of a clinical microbiologist, an information system specialist, an infection control professional, and hospital epidemiologist being optimal (http://cid.oxfordjournals.org/content/44/2/159.full)
Purpose	'…implementation of strategies for EU health systems to support and promote the prudent use of antimicrobials' For consistency and clarity. Add: '…the prudent use of antimicrobials in human medicine.'
International	'International collaboration on surveillance of antimicrobial consumption and antimicrobial resistance [expert consensus].' The One Health dimension should be underlined. Add: 'and antimicrobial resistance in both human and veterinary medicine sectors' HOW international collaboration should take place in respect to surveillance of antimicrobial consumption and resistance should be more fully described at this point. E.g. via mandatory data reporting to the ECDC? As EAHP understands the present situation, not all European states are conducting such reporting to equivalent standards. This section of the guidelines appears an opportunity to address this issue.
International	'Ensure access to essential antimicrobials by supporting market availability [expert consensus].' EAHP research suggests antimicrobials are amongst the category of medicine most frequently in shortage. The Guidelines should make very clear that this problem must be tackled at the international level as part of the effort to combat antimicrobial resistance. More information here: http://www.eahp.eu/press-room/patients-suffering-medicines-shortages-all-european-countries Add: 'by supporting market availability and tackling shortages'
International	The recommendations, and expert opinion, of the O'Neill Report appear underrepresented in this section. http://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf Add: - Develop, support and highlight international public awareness campaigns (including targeting children, teenagers, students, the elderly and vulnerable groups) - Enhance global collaborations in achieving successful research into new microbiological agents Aim for the development, support and implementation of international political agreements on tackling antimicrobial resistance
International	This issue is not represented in the current guidelines. Add: 'Develop European evidence-based guidelines on the use of allergy testing for patients with a history of allergic reaction to beta-lactams and ensure access to these testing kits.'
International	Divergent approaches towards surveillance appears to be an existing problem in the antimicrobial resistance landscape within the EU at present. For example, some EU initiatives in the area of surveillance are not yet able to collect data from all EU countries. The Guidelines section dealing with international principles appears an appropriate section to highlight this issue in need of resolution. Add: 'In respect to surveillance, oversight and standards are required to insure against divergence of approach, methodology and reliability' REF: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/04/news_detail_002507.jsp&mid=WC0b01ac058004d5c1
National and regional	'Ensure availability of standardised local and national open data for benchmarking [expert consensus].' EAHP also suggest some further information be provided as to what is meant by 'standardised local and national data for benchmarking'. One presumes it refers to surveillance data on antimicrobial use and resistance, but this is not explicitly clear. Add: 'local and national open data for benchmarking, in accordance with European and international norms.'
National and regional	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7].' The lists can only be effective if all relevant actors have strong awareness of their existence. Modify: 'Establish, publish and promote awareness of, a list of antimicrobials with restrictive measures for use.'
National and regional	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8].' Achieving public accountability for the actions necessary for achieving prudent use must be understood as an important objective of the guidelines Add at end: 'In order to obtain accountability for this vital aspect of prudent use, chief responsibility for achieving public awareness should be ordinarily understood to be the responsibility of the national health ministry'

Section of document	Comment and rationale – proposed change
National and regional	'Promote the introduction of electronic antimicrobial prescribing systems able to link clinical indication, microbiological and consumption data [expert consensus].' 'Promote' is too weak. Without electronic prescribing systems, antimicrobial stewardship programmes are handicapped. Modify: 'Ensure and monitor the introduction of electronic antimicrobial prescribing systems'
National and regional	'Promote common antimicrobial stewardship programmes covering hospitals, primary care and long-term care facilities at national and regional level [expert consensus].' 'Promote' is too weak. If Europe is serious about achieving prudent use, antimicrobial stewardship programmes are a 'must have'. Modify: 'Ensure and monitor common antimicrobial stewardship programmes'
National and regional	Responsibilities for prudent use within the healthcare system need to be assigned and clearly communicated in order that individuals understand their roles, and those of their colleague healthcare professionals. Add: 'Define the role of healthcare professionals in delivering prudent use of antimicrobials and ensure training and education systems support these.'
Healthcare facilities	The issue of inter-sectoral partnership is under-represented in the guidelines Add: 'Ensure the hospital- based programmes are adequately resourced to allow integration with the local long-term care facilities and community area'
Healthcare facilities	'An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv).' EAHP suggests consideration be given to including a clinical microbiologist to the essential components of an antimicrobial stewardship team, at least in those countries where the profession exists.
Healthcare facilities	This should be understood as an essential element of an antimicrobial stewardship team. Add: 'An adequately resourced clinical pharmacy service.'
Healthcare facilities	Issues of governance should be represented within the guidelines Add: 'Appropriate governance arrangements with effective senior management support'
Healthcare facilities	'An annual report on antimicrobial stewardship activities' Amend to: 'An annual report of antimicrobial stewardship activities, which includes evaluation of effectiveness'
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment [17-23].' 'Promote' is too weak. Modify: 'Utilise rapid and/or point-of-care diagnostics'
Healthcare facilities	'Establish a multi-faceted approach that may include elements such as clinic-based education, patient information leaflets [25] and public patient education campaigns combined with clinician training [21] in communication skills' This important aspect of antimicrobial stewardship in hospitals is under-described in the guidelines Amend to: 'patient information leaflets, pharmacist counselling of patients on their antibiotic therapy, and public patient education campaigns'
Healthcare facilities	Proper adherence to antibiotic therapy is one of the measures required to prevent antimicrobial resistance. This issue is not covered robustly in the current guidance document. Add: 'Ensure patients are counselled on the importance of adherence and the importance of not sharing any unused antibiotics with others.'
Laboratories	This matter is not currently covered in the draft guidelines Add: 'Ensure healthcare teams have guidance on appropriate sampling.'
Prescribers	'consider relevant host factors: age, immune status, renal function, allergies, foreign bodies and risk factors for antimicrobial resistance (e.g. history of recent antimicrobial use, history of recent travel) [expert consensus]' Important elements missing from consultation draft Add: '…potential drug interactions, hepatic function, pregnancy, breastfeeding, BMI' Amend: change the words 'foreign bodies' to 'prosthetic material'
Prescribers	'Follow guidance for perioperative antimicrobial prophylaxis [43] and, in particular, administer intravenous perioperative antimicrobial prophylaxis within 60 minutes before incision (except when administering vancomycin and fluoroquinolones), prefer single dose of perioperative antimicrobial prophylaxis, and avoid prolonging antimicrobial prophylaxis after the end of surgery [expert consensus]' Matter not currently covered in consultation draft Add: 'with re-dosing intra-operatively if significant blood loss or procedure time extends beyond antimicrobial half-life'
Prescribers	Though it is important that the guidelines clarify the role of different healthcare professionals, it is also important that the points of interaction are also described in order to support the team response. Add: 'Advice on dose selection and drug concentrations should be obtained from the hospital pharmacists'
Pharmacists	In the preamble, the role of the pharmacy in both hospital and community settings, in advising other healthcare professionals on antimicrobial matters, is greatly under-described in the current guidelines. Amend to: 'Pharmacists, in both community and hospital settings, are ideally placed to promote the prudent use of antimicrobials and can act as an important source of advice and information to patients, prescribers, nurses and other healthcare professionals. As such, pharmacists must be provided with appropriate training, guidelines and information in order to exercise their stewardship role to the fullest extent possible.'

Section of document	Comment and rationale – proposed change
Pharmacists	EAHP recommends strong revision of section 6. Firstly, the role that the pharmacist can contribute to achieving prudent use is under-described. Secondly, similar to descriptions in the prescriber section (i.e. 'in the community' and 'in the hospital') making a distinction for the role of pharmacists in different settings will add further value and clarity to the document. Clear understanding of healthcare professional roles in achieving prudent use must be understood as an important objective to be achieved by these guidelines. EAHP makes suggestion for the described role of the pharmacist in the hospital setting, but also suggest ECDC consult closely with other representative organisations for pharmacists in order to ensure accurate description of the pharmacist role in achieving prudent use in other sectors. For example, the core role of the community pharmacist. EAHP suggests additional wording: 'In the hospital setting, as described in section 3, the pharmacist is an essential component of the antimicrobial stewardship team. The role of the pharmacist in the hospital setting in respect to achieving more prudent use of antimicrobials should be understood as including: • reviewing antibiotic duration; • advising on the cessation of inappropriate antibiotic treatments; • counseling on restricted use of certain antibiotics; • advising on dosage, preparation and administration, especially for specialised patient cohorts such as children • advising on appropriate disposal policies • educating other healthcare professionals on the restricted use of certain antibiotics, as well as other aspects of antibiotic use such as dosing, preparation, and administration; and, • counseling patients on the use of their medicines, including the importance of completing antibiotic therapy even when symptoms recede.
Nurses	The role of nurses within the clinical team, and in particular their regular contact with patients and their role in administering medicines, can be critical to ensuring that antimicrobials are taken according to the prescription and for monitoring the response to antimicrobials (including potential adverse effects).' Alongside pharmacists, prescribers and others, nurses are key contributors to antimicrobial stewardship in hospitals. Amend to: 'The role of nurses within the clinical team, and in particular their regular contact with patients and their role in administering medicines, is critical to ensuring that antimicrobials are taken according to the prescription'
Nurses	'Be actively involved in antimicrobial management as part of the clinical team by acting as the link with the pharmacy, being responsible for the administration of antimicrobials and for monitoring the patient and patient safety [expert consensus].' This does not occur to EAHP as the optimal chain of communication. Prescribers, nurses, pharmacists, and other healthcare professionals are all equal components in antimicrobial management. Delete: 'by acting as the link with the pharmacy'
Public/patients	This environmental aspect is under-emphasised in the guidance. Add: 'Dispose of unused antibiotics responsibly and do not share with others e.g. family or friends'
Public/patients	Proper adherence to antibiotic therapy is one of the measures required to prevent antimicrobial resistance. This issue is not covered robustly in the current guidance document. Add: 'Complete the full course of prescribed antibiotic therapy, even when symptoms recede'
Public/patients	Further information here: https://www.fip.org/files/fip/publications/2015-11-Fighting-antimicrobial-resistance.pdf Add new sentence: 'Education to patients/the public about prudent use and the importance of completing prescribed antibiotic courses, should be complemented by direct counselling from pharmacists e.g. at discharge from hospital, on collection of prescription.'
Research	'Promote research on interventional studies for antimicrobial prescribing [expert consensus]' 'Prescribing' is too narrow a field of description in terms of research needs. Amend to: 'Promote research on interventional studies for antimicrobial prescribing, as well as other important facets of understanding such dosing, administration, interactions and patient understanding'
Research	Many healthcare professionals are very engaged in innovative and interesting projects connected to combating antimicrobial resistance. However, EAHP surveys have found that often the professional is not encouraged by their management or health system to publish findings. Add: 'Encourage all healthcare professionals to participate in research projects, and to publish and share results, supporting with appropriate training and education opportunities.' http://www.eahp.eu/publications/survey/content/2015-survey
Research	European coordination is required. Add: 'In order to facilitate the exchange of best and good practices, and research, a central online European repository for research and practices in respect to prudent use should be established, with mandate and funding assigned to ensure its sustainability and success.'
Research	This will assist better tuning of the antibiotic medicine to the patient. Add: 'Reevaluation of the Pharmacokinetic/Pharmacodynamic profile of older antibiotics'

Section of document	Comment and rationale – proposed change
References	EAHP highlights the following further references to the Guideline authors: EAHP policy statement on antimicrobial resistance http://www.eahp.eu/practice-and-policy/antimicrobial-resistance ASHP Statement on the Pharmacist's Role in Antimicrobial Stewardship and Infection Prevention and Control https://www.ashp.org/DocLibrary/BestPractices/SpecificStAntimicrob.aspx Canadian Society of Hospital Pharmacists' Statement on the role of the pharmacist in antimicrobial stewardship. http://www.cshp.ca/dms/dmsView/1_Antimicrobial-Stewardship-Statement-FINAL.pdf Antimicrobial Stewardship from Policy to Practice: Experiences from UK Antimicrobial Pharmacists http://link.springer.com/article/10.1007/s40121-015-0080-z CDC: Core Elements of Hospital Antibiotic Stewardship Programs http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html Australian Commission on Safety and Quality in Healthcare: The role of the pharmacist in antimicrobial stewardship. http://www.safetyandquality.gov.au/wp-content/uploads/2012/02/37739-Pharmacist-Role.pdf A qualitative study of hospital pharmacists and antibiotic governance: negotiating interprofessional responsibilities, expertise and resource constraints http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4744423/ FIP: The contribution of pharmacists to fighting antimicrobial resistance: https://www.fip.org/files/fip/publications/2015-11-Fighting-antimicrobial-resistance.pdf WHO Europe: The role of pharmacist in encouraging prudent use of antibiotics and averting antimicrobial resistance: a review of policy and experience http://www.akilciilac.gov.tr/wp-content/uploads/2015/01/dso-ecza.pdf
Appendix	EAHP suggests an indicator be added to measure the level of public and healthcare professional awareness
European Committee for Homeopathy (ECH) (Belgium)	
National and regional	45.000 EU doctors practice homeopathy, especially in respiratory tract infections (RTI). They use less antibiotics in RTI: (OR=0.43, 95% CI: 0.27–0.68). Grimaldi-Bensouda L. PloSone 2014 Add: 'Consider alternative interventions to reduce inappropriate antimicrobial prescribing.' - Ref: Grimaldi-Bensouda L, Bégaud B, Rossignol M, et al. Management of upper respiratory tract infections by different medical practices, including homeopathy, and consumption of antibiotics in primary care: the EPI3 cohort study in France 2007-2008. PLoS One. 2014;9(3):e89990. doi:10.1371/journal.pone.0089990.
Research	There are more than 20 randomised controlled trials of homeopathy in respiratory tract infection. One meta-analysis (Shang, Lancet 2005) concludes, based on 8 trials: 'substantial beneficial effect (odds ratio 0.36, [95% CI 0.26-0.50]) in acute upper respiratory tract infection'. One review, based on 3 trials (NHMRC, 2015) concludes: 'Based on the body of evidence evaluated in this review homeopathy is not more effective than placebo for the treatment of people with upper respiratory tract infection'. Add: 'Support and promote research into alternatives to antimicrobials.' (This is consistent with 'Guidelines for the prudent use of antimicrobials in veterinary medicine (2015/C 299/04)') - Ref: Shang A, Huwiler-Müntener K, Nartey L, et al. Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. Lancet. 2005;366(9487):726-732. doi:10.1016/S0140-6736(05)67177-2. - National Health and Medical Research Council. 2015. NHMRC Information Paper: Evidence on the effectiveness of homeopathy for treating health conditions. Canberra: National Health and Medical Research Council; 2015.
European Federation of Nurses' Associations (EFN) (Belgium)	
Introduction	This is the first mention, but throughout the focus remains largely on 'medical practice'. This places unnecessary pressure and responsibility on the medical profession, while implying other actors have only a supportive function to doctors. This conflicts with the recommendations to an interprofessional team approach to responding to the AMR challenge. Refer to: healthcare practice
National and regional	Additional recommendations would be prudent here Add: 'Support the development of non-medical prescribers to contribute to antibiotic stewardship' 'Prevent the risk of excessive antibiotic use in hospitals, through investing in nosocomial infection prevention systems' 'Amend legislative/regulatory frameworks where required to facilitate the advancement of nursing and midwifery practice to include prescriptive authority.' 'Fund the development of nursing and midwifery education programmes which will permit nurses and midwives to make prescribing decisions'
Healthcare facilities	A key recommendation appears missing here Add: 'Support clinicians to gain the necessary training and expertise to support the antimicrobial stewardship team'
Nurses	As the ones who actually deliver patient care, nurses are critical to ensuring that antimicrobials are taken according to prescription and for monitoring patient response Modify: 'The role of nurses within the clinical team, and in particular their regular contact with patients and their role in administering medicines, is critical to ensuring that antimicrobials are taken according to the prescription…'
Nurses	Add in the following 2 points: 1. Fund the development of nursing and midwifery education programmes enabling nurses to undertake leadership roles as infection control practitioners 2. Recognise infection control nurses as specialist experts
Education/ academics	Add: 'Develop and offer non-medical prescribing courses via flexible learning routes'
Research	Given the plethora of research reports that remain in obscurity, an important recommendation is missing. Add: Ensure that available research is properly amalgamated and synthesised through systematic reviews and meta-analyses, to inform clinical guideline development and decision making
Pharmaceutical industry	A considerable number of research reports undertaken/commissioned by pharmaceutical companies remain unpublished. Add: 'Commit to making results of antimicrobial trials publicly available.'

Section of document	Comment and rationale – proposed change
European Federation of Pharmaceutical Industries and Associations (EFPIA) (Belgium)	
General	Vaccines play a key role in preventing the use of antibiotics by reducing (both bacterial and viral) infections, thereby limiting the use of antibiotics. Guidelines on the prudent use of antimicrobials in human medicines ought to make sure that this preventative intervention is recognised and promoted, not least against the background of the 2014 Council conclusions on vaccination. Therefore EFPIA strongly supports the comments made in the submission by Vaccines Europe
	To account for international efforts to tackle antimicrobial resistance, EFPIA would suggest that consideration should be given to the alignment of this section with the 7 core elements of hospital stewardship programmes promoted by the U.S. Centres for Disease Control and Prevention (in so far as is possible)
	Given the prescriptive nature of some of the recommendations contained within section 5 and the fact that some of the desired actions span multiple disciplines, particularly pharmacy, it is suggested that clarification be provided so as to make it clear that the recommendations span professions. Currently the sections relating specifically to pharmacists, nurses and infection control practitioners look under-developed by comparison.
Section 8	What does 'infection prevention' mean? Provide definition
Introduction	'The exposure of microorganisms to antimicrobial agents creates the selective pressure that leads to the development of resistance' Exposure of micro-organisms to antimicrobial agents is not the only form of selective pressure that selects for resistance to antimicrobials. The best example is the induction of efflux pumps by conditions other than drug exposure. 'The' should be changed to 'a' since we know of examples of resistance mechanisms that are selected for in the *absence* of exogenous antimicrobial pressure, but which nevertheless result in shifts in antimicrobial susceptibility. 'The exposure of microorganisms to antimicrobial agents creates a selective pressure that leads to the development of resistance.'
International	'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns to support appropriate antimicrobial use [expert consensus].' It is suggested that this line be modified to distinguish between what is appropriately handled at the international level (the sharing of intelligence, surveillance data and best practice strategies), as opposed to the national level (design and implementation). Modify: 'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and the active sharing of national design and implementation strategies and campaigns to support appropriate antimicrobial use'
International	'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns to support appropriate antimicrobial use [expert consensus].' 'Establish a new European platform for sharing best practice interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes [expert consensus].' Expand these lines to include campaigns to reduce inappropriate antibiotic use, not just '.. support appropriate AMR use..' and to share best practice (with supporting data on outcomes) on reduction. In Denmark, for example, they have a very well-monitored program to reduce antimicrobial use in agriculture which was able to demonstrate dramatic reductions in use, after changes to the regulations without negative outcomes. That kind of solid data gathering is needed to reassure prescribers that controlling prescription will not harm patients. Modify: 1.'International and European collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns support appropriate antimicrobial use and *reduce inappropriate antibiotic use* [expert consensus].' 2. 'Establish a new European platform for sharing best practice *(with supporting data on outcomes)* interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes [expert consensus].' Add: 3. 'support further development of the evidence base underpinning the 'one health approach' and standardized approaches to the assessment of outcomes'
International	New point: important aspect of harmonisation Work with US authorities to progress harmonised clinical breakpoints (specifically a common approach between CLSI for the US and EUCAST for the EU) as well as harmonized methods for antimicrobial susceptibility testing
National	'Fund, develop and implement a national action plan for appropriate use of antimicrobials in human medicine including multi-faceted interventions adapted to local conditions [1] [expert consensus].' This should be expanded to explicitly include reduction of inappropriate antibiotic use as a goal. Modify: Fund, develop and implement a national action plan for the reduction of inappropriate use of antimicrobials in human medicine including multi-faceted interventions adapted to local conditions
National	'Set qualitative and quantitative targets for improvement of prescribing [expert consensus]. Example: antibiotic quality premium (NHS England) [2].' Setting qualitative and quantitative use for antibiotics should also be supported by improvement Set qualitative and quantitative targets for improvement of antibiotic prescribing and vaccination coverage.
National	Ensure timely publication of national and ECDC AMR reports Add new bullet: 'Ensure national and ECDC AMR evolution reports are published in a timely fashion'
National	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7].' Restriction can be an effective means to help control an outbreak of resistance; however EFPIA would query the need to include this as a required element of the ECDC guideline. If inclusion is deemed necessary then the recommendation could be strengthened by including clarification on where and when this may be appropriate. Establish guidance as to the circumstances under which use restriction may be appropriate, the procedures to be adopted and the adaptation to local epidemiology
National	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8].' suggest clarification of this line to reference 'education' specifically. National campaigns for antibiotic use should also be supported by national campaigns for increased vaccination uptake. Suggest amending this bullet as follows: 'Give high priority to the Funding, design, implementation and assessment of national educational campaigns on antimicrobial use and vaccination targeting the public and health professionals'
National	'Explore per unit dispensing of antimicrobials to match pack size with planned course duration according to national guidelines [expert consensus].' Per unit dispensing should be reconsidered in view of the significant legal and regulatory implications in terms of Good Distribution Practices, implementation of the Falsified Medicines directive (traceability, risks of counterfeited medicines), etc. Replace existing bullet with: 'Set up joint stakeholder group to explore per-unit dispensing, in particular to assess the specific contribution to conservation that would be made against the resources required'

Section of document	Comment and rationale – proposed change
National	'Supervise and regulate promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing [expert consensus].' 1) Promotional activities are already strictly regulated, thus making sure that they are strictly limited to the Summary of Product Characteristics (SPC) of a medicine. 2) In addition to the existing EU and national framework, the EU research-based pharmaceutical industry (EFPIA) and the generic industry (Medicines for Europe) have established codes regulating promotional activities and interactions with healthcare stakeholders Appropriate promotional activities ought to be an essential part of any policy aiming at avoiding misuse of antibiotics. As such, these activities need to be very well aligned to appropriate use. Specifically, activities that may lead to increased use should be avoided. However, the most practical and efficient mechanism to do this and the objective need careful consideration, in order to ensure that prescriber/producer interactions remain possible while eliminating inappropriate practices, and we suggest a working group is set up with industry and relevant stakeholders to develop a proposal. Replace existing bullet with: 'Work with the pharmaceutical industry to identify best practices on antibiotic promotional activity to ensure it aligns with the goal of advancing antimicrobial stewardship'
Prescribers	'Prescribers are ultimately responsible for the decision to use, and the choice of, antimicrobials in patient care, and as such need to be provided with appropriate training, guidelines and information in order to be able to exercise prudence in the prescribing of antimicrobials and manage patient expectations' While prescriber training is mentioned in the preamble to this section, it should be emphasized. They ultimately control access to antibiotics in most countries, and they need to feel a personal stake in this issue. It's not enough that institutes offer training programs: prescribers (and their professional societies) need to feel that they have an obligation to be educated and proactive on the issue of AMR). Also, in this section, 'prescribers' is used as a synonym for doctors – but pharmacists and nurses (covered, albeit briefly in sections 6 and 7) are also often prescribers and have the same need for training and ownership. Modify: 'Prescribers are ultimately responsible for the decision to use, and the choice of, antimicrobials in patient care, and as such need to be provided with appropriate mandatory and regular training, guidelines and information in order to be able to exercise prudence in the prescribing of antimicrobials and manage patient expectations. Training courses should be constructed with professional societies and include physicians, nurses and pharmacists. They ought to be constructed in a way that guarantees that prescribers understand the need for constant training.'
Prescribers	Prescribers should follow their national infection control policies in reducing dissemination of infections including prevention by vaccination. Suggest new bullet in the community section: 'Prescribers should follow their national infection control policies in reducing dissemination of infections including prevention by vaccination.'
Prescribers	Additional point 'In all clinical contexts, prescribers should provide follow-up and record outcomes of treatment'
Pharmacists	'Do not dispense antimicrobials without prescription, unless specific provisions allow for regulated dispensation in specific circumstances [expert consensus]' As a principle, antibiotics should be available upon prescription only. Any exceptions should be clearly defined (eg. Public health threats). Modify: 'specific' with 'extraordinary'.
Education	'Ensure that all healthcare professionals are regularly trained on appropriate antimicrobial use [14,46].' Strategies for *reducing* inappropriate antibiotic use' should also be included Add: '..and on strategies for reducing inappropriate antibiotic use'
	'Example: require participation in a minimum number of certified education activities on antimicrobial prescribing and use' Importance that all providers also understand the appropriate use of vaccines and the role they play in minimizing unnecessary use of antibiotics. Suggested edit: 'require participation in a minimum number of certified education activities on infection prevention and control, and more specifically on antimicrobial prescribing and use and vaccine use.'
Research	Chapeau text should reflect the need for sustained R&D investment. Add: 'Sustained public, government, industry and philanthropic investment in basic, translational and clinical research into infectious diseases and their prevention, as well as research into the discovery and development of novel antimicrobials, are all essential components in combating antimicrobial resistance.'
Research	Underline the importance of public-private partnerships and collaboration Add a new sentence: 'Research collaboration and partnership between the public and private sectors are key to address these challenges'.
Research	Consideration should be given by the ECDC to expand this section on research recommendations to include reference to: • Risk stratification of patients • Real world outcomes research • Use of electronic clinical decision support New bullets to promote research into: 1. Risk stratification of patients 2. Real world outcomes research 3. Use of electronic clinical decision support
Research	'Research the risk of specific antimicrobials and antimicrobial classes for the selection of antimicrobial resistance in microbiota to allow ranking and rational use [expert consensus]' The word 'ranking' is not clear/confusing. In order to thoroughly study the risk of selecting for resistance among the microbiota one would need to have a means to culture the entire microbiota, and correlate levels of in vitro susceptibility with clinical outcomes. This is not a practical approach to ranking the selection of which drugs should be prescribed over which others. Delete 'ranking' or add a definition
Research	Points missing to give a full picture of research needs Add the following bullets: promote research in preventive measures and tools that will reduce our dependence on antibiotics, including 1. improved infection control 2. vaccines against community and hospital acquired infections and viral or parasitic infections 3. rapid and point-of-care diagnostics 4. evidence-based guidelines for the role of diagnostics in appropriate antimicrobial prescribing

Section of document	Comment and rationale – proposed change
Research	Important that incentives support early stage R&D through market-based incentives, consistent with the 'Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance' Add new bullet: 'Support development of novel incentive policies that improve financial and access-related predictability to ensure sustainable investment in new antibiotics, vaccines, and diagnostics'
Pharmaceutical industry	'Adapt pack size and strength to indications [14] [expert consensus]' 1) Patient's consumption of a given number of units (e.g. tablets) of antibiotics shouldn't depend on package size but on doctor's ordinance (via prescription). Industry is not in a position to predict all potential therapeutic schemes which could be prescribed by doctors in each individual case, and adjust upfront packages of all units as well as the strength of the active substances. Due to the above mentioned difficulties, the technical feasibility of implementation of such a change is very low. 2) Such a proposal would lead to the creation of a significant number of different packages and strengths of the active substances, which could increase the risk of drug shortages in the antibiotics area, thus putting patients' health at risk. 3) Changing packages and the strength of the active substance might have legal and regulatory implications, since this may require manufacturers to conduct new clinical trials, and request new marketing authorizations, etc., which represent a high burden for the manufacturers. This type of proposal should be subject to a thorough impact assessment evaluating the legal (pharmaceutical regulatory framework), economic and public health implications, before being further discussed. In conclusion, this proposal may have unintended consequences, and the cost of the proposed adjustment could be disproportionally significant vs. the potential healthcare benefits. Delete this recommendation
Pharmaceutical industry	'Consider special labelling of antimicrobial packages that identify them as such and indicate that they are medical products for specific use only as prescribed [expert consensus]' 1) In principle, antibiotics should be available upon prescription only and the additional labelling of packages will not influence doctors' therapeutic decision regarding the number of units being prescribed (e.g. tablets). 2) The proposal should be also reviewed in light of antibiotics dispensed in hospital settings (e.g. surgery) where patients are not in contact with antibiotic packages (and would not be able to notice any additional warning information). Prescribers should give clear instructions on how to take the treatment and inform patients about the risk of antimicrobial resistance associated with the inappropriate use of antibiotics. Delete this recommendation
Pharmaceutical industry	Suggested new sub-paragraphs to further underpin the statement in respect to the industry as a 'key partner' suggest adding the following subparagraphs: 1. Encourage, when conducting promotional activities (and where relevant, appropriate and permitted) the adoption of diagnostic technologies that are designed to facilitate faster diagnosis and identification of optimal treatment regimens 2. When engaging with payers and prescribers, aid (where appropriate, relevant and permitted), the dissemination of educational materials produced by national public health agencies 3. Engage with national and international policy-makers to support the development of policies that promote appropriate antimicrobial prescribing, including the design of novel reimbursement systems and processes that contribute to the goals of access and conservation
European Institute of Women's Health (EIWH) (Ireland)	
Healthcare facilities	'Monitoring of quality indicators and quantity metrics of antimicrobial use with feedback to prescribers and prescriber actions agreed. Example of indicators: defined daily doses (DDDs) or days of therapy (DOTs) per 100 patient-days; proportion of cases of *Staphylococcus aureus* bacteraemia where infectious disease consultation was provided.' All data collected should be disaggregated by sex and gender as well as for age. Add 'disaggregating data by sex/gender and age'
Healthcare facilities	'Establish a multi-faceted approach that may include elements such as clinic-based education, patient information leaflets [25] and public patient education campaigns combined with clinician training [21] in communication skills.' Information should target all health-decision-makers. For example, with regard to children, parents or other caregiver typically maker the decisions for care. Target audiences should include healthcare managers. Suggested changes: 'patient information leaflets' should be changed to 'patient and carer information leaflets': 'public patient education campaigns' should be changed to 'public education campaigns'
Prescribers	'consider relevant host factors: age, immune status, renal function, allergies, foreign bodies and risk factors for antimicrobial resistance (e.g. history of recent antimicrobial use, history of recent travel) [expert consensus]' 'Sex/gender considerations must be incorporated into healthcare decision-making, including the consideration for women who are pregnant or breastfeeding. Add: sex/gender, pregnancy/breastfeeding status
Prescribers	'inform the patient about their antimicrobial treatment' Information should target all health-decision-makers, including caregivers and family who serve as health gatekeepers and/or provide care, particularly for children. Change 'the patient' to 'the patient, their caregivers and/or their family'
Prescribers	'consider delayed antimicrobial prescribing with appropriate safety netting for adults or children in specific circumstances and according to guidelines [36-38]. Example: delayed antimicrobial prescribing for upper respiratory tract infections' Consideration for the health of the mother and child should be taken with regard to the use of antimicrobials. Add 'and other groups, such as women who are pregnant or are breastfeeding'
Pharmacists	'Pharmacists are the gatekeepers to the use of antimicrobials and can act as an important source of advice and information for patients, and as such need to be provided with appropriate training…' Families and caregivers play an important role as health gatekeeper as well as managers of healthcare. It is important to ensure they are educated, especially when they play a critical role in health decision-making. 'for patients' should be changed to 'for patients, families and caregivers'
Education/ academics	'Introduce education on prudent antimicrobial use, antimicrobial resistance, vaccination and hygiene in primary and secondary education' 'Third level education offers an additional opportunity to educate the public and future professionals, including relevant future stakeholders including but not limited to healthcare professionals, social workers and teachers. 'primary and secondary education' should be change to 'primary, secondary and third-level education'
Public/ patients	'Current evidence and expert opinion support the following as effective elements of guidelines in respect of the public and patients in the control and prevention of antimicrobial resistance:' Families and caregivers play an essential role in health decision-making and management. Health literacy of patients, carers, families and the general public is vital to combatting antimicrobial resistance. 'the public and patients' should be changed to 'the public, patients, families and caregivers'

Section of document	Comment and rationale – proposed change
Research	'Promote research that assesses and compares behavioural change interventions for antimicrobial prescribing, taking into account cultural differences, in order to improve our understanding of the optimal ways that rational antimicrobial prescribing practices can be achieved [47]' Research should differentiate and be disaggregated for sex and gender differences as well as for age. Topics, such as the safety of antibiotics during pregnancy, breastfeeding and childhood years should be thoroughly studied. 'taking into account cultural differences' should be changed to 'taking into account cultural, sex/gender and age differences'
Research	'Promote high quality clinical research studies on existing antimicrobials' Children, women, older people, minorities and other underrepresented groups should be sufficiently represented in all research and utilised in research evaluation. Add '….ensuring studies sufficiently consider sex/gender and age factors across the lifespan'
European Medical Students' Association (EMSA)	
National and regional	Separating prescribers and sellers/distributors avoids the conflict of interest. ADD: 'Review, or establish if not available, legal provisions to forbid professionals to both prescribe and sell or dispense antibiotics at the same time.'
Education/academics	'Include training on prudent antimicrobial use in medical, nursing, pharmacy, dentistry and midwifery schools [expert consensus] [14,20]' Interprofessional collaboration (IPC) is a key element of healthcare. Interprofessional education (IPE) allows students to acquire knowledge, skills and attitudes that will enable them to work as part of a multidisciplinary team. It provides an ability to share skills and knowledge between professions and allows for a better understanding, shared values, and respect for the roles of other healthcare professionals. CHANGE: 'Include training on prudent antimicrobial use with a strong practical component and interprofessional interaction in medical, nursing, pharmacy, dentistry and midwifery schools.'
European Public Health Alliance (EPHA) and the Royal College of Physicians (RCP)	
Introduction	'Combined with the meagre development of novel antimicrobials, the spread of resistance to existing ones is leading to loss of effective options for the treatment and prevention of infections, representing a global health security threat for Europe.' To ensure that the AMR threat is properly expressed, the global importance should be emphasised too. Rephrase: '(…) security threat for Europe and globally.'
Definitions	'Antimicrobial stewardship programmes refer to a coordinated programmes that implement interventions to ensure appropriate antimicrobial prescribing and effective antimicrobial treatment, to limit antimicrobial resistance and to prevent *Clostridium difficile* infections' Antimicrobial stewardship programmes are not only effective for ensuring appropriate antimicrobial use or correct prescribing practices. Often, they provide the opportunity to teach about AMR as well. Additional writing: '(...) *Clostridium difficile* infections; and implement interventions to educate professionals and the public on the consequences of inappropriate use – and thus on AMR.'
Purpose	'…to support and promote the prudent use of antimicrobials' To ensure clarity of focus Add '(…) promote the prudent use of antimicrobials in human medicine'.
International	'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns to support appropriate antimicrobial use [expert consensus].' The term 'international collaboration' is not further specified, which could lead to difficulty enacting upon it. It should be detailed whether antimicrobial stewardship interventions will be organised at the EU level, or whether it is expected individual countries develop international collaborations with neighbouring countries. Specify the kind of international collaboration that is expected to be established. In case of an EU level initiative, designate an organising entity. In case of member state initiative, specify how and by when such collaborations are expected to be developed, and how their implementation and monitoring can be ensured.
International	'International collaboration on surveillance of antimicrobial consumption and antimicrobial resistance [expert consensus].' As with the previous comment, the term 'international collaboration' is not specified. To ensure data reporting and support for the surveillance of antimicrobial consumption, a European initiative would be recommended. Additionally, the One Health dimension could be underlined here. Additional writing: '... [expert consensus]. Support international collaboration through mandatory data reporting on antimicrobial consumption and resistance – in the human and veterinary medicine sectors – to one EU entity (e.g. the ECDC).'
International	'Ensure access to essential antimicrobials by supporting market availability' Ensuring access to essential antimicrobials is important, as is limiting the use of last-resort antimicrobials to safeguard their effectiveness. Add: '(...) by supporting market availability and tackling shortages. Meanwhile, limit the use of last-resort antimicrobials throughout the healthcare line to safeguard their effectiveness. Link this to the list developed under recommendation 'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7].'
International	The recommendations, and expert opinion, of the O'Neill Report appear underrepresented in this section. http://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf Add: - Develop, support and highlight international public awareness campaigns (including targeting children, teenagers, students, the elderly and vulnerable groups) - Enhance global collaborations in achieving successful research into new microbiological agents - Aim for the development, support and implementation of international political agreements on tackling antimicrobial resistance
International	The various approaches to surveillance appear to be a continuous obstacle in the AMR landscape (European Medicines Agency. (2016). *Collecting high-quality data on antibiotic use in animals in support of the fight against antimicrobial resistance*. Retrieved from http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/04/news_detail_002507.jsp&mid=WC0b01ac058004d5c1) Add: 'In respect to surveillance, oversight and standards, a common EU approach to monitoring, methodology and reliability should be developed.'

Section of document	Comment and rationale – proposed change
National and regional	'Ensure availability of standardised local and national open data for benchmarking [expert consensus].' Though mentioned under the *National and regional* heading, it would be important to allow open data for benchmarking on the international levels too. This could improve international collaborations and benchmarking, allowing to see high-use member states to see how little antibiotics low-use member states dispense – providing incentive for national improvement. Rephrase: '(…) standardised local, national and international open data for (…)'
National and regional	'Ensure national clinical guidance is reviewed and revised when there is a significant change in antimicrobial resistance, new evidence on management of infections or at regular intervals (e.g. 2–3 years) [expert consensus].' Acting upon new information is important: in case there are new resistant microbes present, prescribing practices should be adjusted within a short-time period as should treatment courses. The resistant microbes may affect an entire population within a matter of months. Therefore, it is recommended to set an interval period for updating antimicrobial treatments per 6 months; and review and revise clinical guidance every 1-2 years. Rephrase: 'Ensure antimicrobial treatment courses and healthcare professionals' knowledge are updated every 6 months on the latest developments in the AMR-issue (e.g. through educational trainings). Ensure national clinical guidance is reviewed and revised [...] at regular intervals (e.g. 1-2 years).'
National and regional	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7]' To ensure such a list is used throughout all healthcare related practices, all actors involved should be made aware of its existence. Add: '... [4,6,7]. Publish and promote the list among all relevant stakeholders.'
National and regional	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8].' Students should be involved and targeted in national campaigns, too. Achieving public accountability for prudent use of antimicrobials should also be an important objective. 1. Add: '[…] targeting the public and health professionals [8]. They should be undertaken in collaboration with both professional and student healthcare organisations.' 2. Add at end: 'Chief responsibility for achieving public awareness – public accountability – should be the responsibility of the national health ministry.'
National and regional	'Ensure compliance with the regulations with regards to the dispensing of antimicrobials without prescription and over the internet [expert consensus].' The practice of dispensing antimicrobials without prescription is rather diffuse. Ensuring compliance with regulations with regards to dispensing should therefore apply to all places where antimicrobials can be retrieved (e.g., supermarkets, drug stores, other retail outlets, the Internet) and it would be beneficial to provide examples as to how this can be achieved. Rephrase: '... without prescription (e.g., in supermarkets, drug stores, other retail outlets) and over the Internet [expert consensus]. Ensuring compliance could be enacted through the use of automatic data collection, and limiting availability of antimicrobials in such environments, **other**.'
National and regional	'Promote the introduction of electronic antimicrobial prescribing systems able to link clinical indication, microbiological and consumption data [expert consensus].' 'Promote common antimicrobial stewardship programmes covering hospitals, primary care and long-term care facilities at national and regional level [expert consensus].' The use of 'Promote' is too weak. Electronic prescribing systems are believed to be highly important for the success of antimicrobial stewardship programmes. Similarly, the introduction of stewardship programmes is a 'must'. Rephrase: 1. 'Ensure and monitor the introduction of electronic prescribing systems.' 2. 'Ensure and monitor common antimicrobial stewardship programmes.'
National and regional	Responsibilities for prudent use within the healthcare system need to be assigned and clearly communicated in order that individuals understand their roles, and those of their colleague healthcare professionals. Add: 'Define the role of healthcare professionals in delivering prudent use of antimicrobials and ensure training and education systems support these.'
Healthcare facilities	'An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv).' The antimicrobial stewardship team should include a clinical microbiologist. Add: '(…) at least a clinician (iii), a pharmacist (iv), and a microbiologist.'
Healthcare facilities	'IT support for antimicrobial stewardship activities.' The IT support for antimicrobial stewardship activities can be widespread, thus providing examples would be recommended. Add: '(…) stewardship activities. For example, the development and implementation of RDTs could support prescribing practices and provide teaching opportunities about symptom recognition and infection types. Additionally, electronic feedback on prescribing practices could provide support: these could be professional function specific, infection specific, or antimicrobial specific.'
Healthcare facilities	'An annual report on antimicrobial stewardship activities.' The evaluation should include an evaluation of their effectiveness. Add: '(…) stewardship activities, which includes an evaluation of their effectiveness.'
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment [17-23].' 'Promote' is too weak. Rephrase: 'Utilise rapid and/or point-of-care diagnostics'
Healthcare facilities	'Establish a multi-faceted approach that may include elements such as clinic-based education, patient information leaflets [25] and public patient education campaigns combined with clinician training [21] in communication skills' The multi-faceted approach may also include use of posters in healthcare settings, and antimicrobial stewardship in hospitals. Rephrase: '... information leaflets [25] and posters in healthcare settings, pharmacist counselling of patients on their antibiotic therapy, and (…).'

Section of document	Comment and rationale – proposed change
Healthcare facilities	Proper adherence to antibiotic therapy is required to prevent AMR. The EU should be encouraging all countries to produce a report following the ESPAUR model initiated by Public Health England, which outlines both antimicrobial use and drug bug combinations (see https://www.gov.uk/government/news/espaur-report-reveals-continued-rise-in-antibiotic-resistant-infections) Add: 1. 'Ensure patients are counselled on the importance of adherence.' 2. 'Enable the production of national reports based on healthcare facility data collected on antimicrobial use and drug-bug combinations.'
Healthcare facilities	The term 'clinician' is not clear, it should be clear that this also includes nurses. Either rephrase to make it more clear that nurses are included, or define the term 'clinician' as part of the definitions.
Prescribers	'avoid antimicrobial treatment when there is evidence of viral infection or of a self-limiting bacterial infection [expert consensus]' It is not antimicrobial treatment in general that should be avoided for 'viral infections or of a self-limiting bacterial infection', but antibacterial. Rephrase: 'avoid antibiotic treatment when there ...'
Prescribers	'select an antimicrobial with a spectrum of activity as narrow as possible. Example of indicator: [expert consensus] consumption of beta-lactamase-sensitive penicillins (ATC code: J01CE) expressed as a percentage of the total consumption of antibacterials for systemic use (ATC code: J01) [30]' Prescribers need access to have access to effective diagnostic tools. Add: '… Ensure prescribers have access to effective diagnostic tools.'
Prescribers	'if antimicrobial treatment is not considered necessary, give patients advice about the expected natural history of the illness, the limited or absent benefit of antimicrobial treatment, and the potential unwanted side-effects of antimicrobials such as diarrhoea and rash, as well as advice about actions in case of worsening clinical condition (safety netting)' If antimicrobial treatment is not necessary, and healthcare professionals are asked to provide the patient with advice on the course of the disease, etc., this would also be an opportunity to emphasise the consequences of unnecessary use and AMR. Add: '...of antimicrobial treatment, the potential unwanted side-effects [...], and the consequences of unnecessary use of antimicrobials and the aggravation of the AMR situation.'
Prescribers	In addition to the given recommendations, it would be beneficial to introduce an obligatory check-up period after the administering of an antimicrobial treatment (e.g. every 24h, after 48 hours or after 72 hours). This to customise the antimicrobial treatment where applicable in a timely manner, with the ultimate goal of lowering the amount of antimicrobials administered, ensuring their effectiveness and decreasing the chance of resistance development. Add: 'introduce an obligatory check-up period after the administering of an antimicrobial treatment (e.g. every 24h, after 48 hours or after 72 hours), to customise treatment options where possible within a short timeframe.'
Pharmacists	Pharmacists, being the gatekeepers to the use of antimicrobials, also act as an important source of advice and information, and they must be supported in their practice with appropriate training and tools. Add/modify: 'Do not dispense antimicrobials without prescription, unless specific provisions allow for regulated dispensation [expert consensus]. Advise dosage and administration for treatments, especially for specialised patient cohorts such as children.' 'Ensure that the patient understands the dosage and duration of treatment to improve adherence and increase treatment success; promote appropriate disposal of leftover antimicrobials [expert consensus] (Disposal of Medicines in Europe. (2016). Retrieved from http://medsdisposal.eu/) 'Ensure that the patient understands how to benefit most from their treatment, recognise side effects and know what action to take and know what action to take when a suspected ADR occurs.' 'Ensure the patient understands regulations/advice on the appropriate disposal of medications.' 'Participate in local, regional or national public health campaigns concerning the prudent use of antimicrobials' 'Be actively involved in antimicrobial management in multidisciplinary care teams.' 'Provide counselling on the cessation of antibiotic treatment and on restricted use of certain antibiotics.'
Nurses	For nurses, too, it would be important to receive professional support through active involvement in antimicrobial stewardship programmes and related training. Nurses also contribute to decision-making on the use of antimicrobials as the healthcare worker group most likely to obtain patient microbiology specimens. Add: 'Support antimicrobial stewardship programmes for nurses, to educate them accordingly on the most recent guidelines for administering antimicrobial treatment.' 'Include educational support for nursing staff in the collection, transportation and analysis of microbiology results to support appropriate prescribing strategies.'
Infection control practitioners	'Infection control practitioners play an essential role in the prevention of healthcare-associated infections, many of which are associated with inappropriate antimicrobial use…' The role of infection control practitioners should not only be specified to healthcare-associated infections, but should where possible, be widened to national prevention and control of infections. Therefore, their activities should be supported throughout the healthcare line and internationally, by e.g. the ECDC. 1. Rephrase the introducing paragraph of the infection control practitioners to take account that their function comprises more than infection control including prevention, education and other tasks. For example: 'Infection control practitioners play an essential role in the prevention and control of infections nationwide, many of which are associated with [...]' 2. Add: 'Support the infection prevention and control practices on a local, national and international level, through e.g. stewardship programmes, through funds and infection control conventions for both the public and healthcare professionals'
Education/academics	1. 'Ensure that all healthcare professionals are regularly trained on appropriate antimicrobial use [14,46]. Example: require participation in a minimum number of certified education activities on antimicrobial prescribing and use' The education of healthcare professionals should be regularly updated, i.e. every 1-2 years. Rephrase: '...regularly trained (with biannually updated training programmes) on appropriate ...' 2. 'Introduce education on prudent antimicrobial use, antimicrobial resistance, vaccination and hygiene in primary and secondary education. Example: through implementation of the e-Bug platform [expert consensus].' Different groups of healthcare students should benefit from inter-professional education and training opportunities. Add: '[…] through implementation of the e-Bug platform [expert consensus]. Such education and training opportunities should allow for inter-professional collaboration and interaction with other healthcare students, academics and public health authorities'.

Section of document	Comment and rationale – proposed change
Public/patients	There is also a need to inform the public more on basic hygiene precautions to avoid infections. Throughout the EU, there are many levels in public awareness on the AMR issue (Commission. (2012). *Εθνική Στρατηγική Κύπρου για την Αντιμετώπιση της Μικροβιακής Αντοχής στα Αντιβιοτικά* [*Cyprus National Strategy to Combat Antimicrobial Resistance to Antibiotics*]. Retrieved from http://bit.ly/1VITnQM; Schippers, E.I., Rijn, M.J. van, Dijksma, A.M., Mansveld, W.J. (2015c). *Letter to parliament about the approach to antibiotic resistance.* (Reference 767152-136545-PG). The Hague: Ministerie van Volksgezondheid, Welzijn en Sport). To improve this situation, the EU recommendations should call for support for national awareness campaigns, in addition to the European Antibiotic Awareness Day organised by the ECDC. Add: 1. 'Get informed about appropriate hygiene measures, antimicrobial use […]' 2. 'Support national awareness campaigns, in addition to the European Antibiotic Awareness Day, making use of all available media to raise awareness on AMR and the consequences of inappropriate use.'
Public/patients	'Do not use leftover antimicrobials [expert consensus].' In addition to calling for 'not using leftover antimicrobials', it would be helpful to ensure such leftover antimicrobials are not available for use, by promoting to return them to pharmacies, or other local collection points. Add/modify: 1. 'Promote the return of leftover antimicrobials to pharmacies and local collection points (at local, national and international level) to reduce unnecessary and inappropriate use of antimicrobials among the general public.'
Public/patients	Proper adherence to antibiotic therapy is one of the measures required to prevent AMR. Add: 2. 'Ensure patients understand the importance of completing a treatment course, even when symptoms recede.'
Research	'Promote research on interventional studies for antimicrobial prescribing [expert consensus]' 'Prescribing' is too narrow a field of description in terms of research needs. Rephrase: 'Promote research on interventional studies for antimicrobial prescribing, as well as other important facets of understanding such as dosing, administration, interactions and patient understanding.'
Research	All relevant healthcare professionals should be encouraged to engage in research projects related to tackling AMR. Add: 'Encourage all healthcare professionals to participate in research projects, and to publish and share results, supported by appropriate training and education opportunities'.
Research	European coordination is required for research initiatives. Add: 'In order to facilitate the exchange of best practices and research, a central online European repository for research and practices in respect to prudent use should be established, with mandate and funding assigned to ensure its sustainability and success.'
Research	To assist better tuning of the antibiotic medicine to the patient, older antibiotics should be considered. Moreover, to avoid having to resort to antibiotics more than is necessary, research into alternatives to antibiotics should be explored with more determination (See for example EUROCAM (2015). *The role of Complementary and Alternative Medicine (CAM) in reducing the problem of antimicrobial resistance*. Retrieved from: http://www.cam-europe.eu/dms/files/Position_Papers/EUROCAM_PositionPaper_CAM_and_AMR_November2015.pdf). This would also be consistent with the 'Guidelines for prudent use of antimicrobials in veterinary medicine (2015/C 299/04). Add: 1. 'Re-evaluate the Pharmacokinetic/Pharmacodynamic profile of older antibiotics. 2. 'Support and promote research into alternatives to antibiotics'
GlaxoSmithKline (GSK) (United Kingdom)	
Purpose and Scope	The purpose of the guidelines is only focused on the 'prudent use of antimicrobials' and as such is too narrow The guidelines should also describe and encourage the use of other measures and tools that will contribute directly or indirectly to reducing the use of antimicrobials, largely by preventing infection. These measures need to be used together with the prudent use for optimal effect. Another option is to produce a separate guideline on 'strategies and tools to address AMR by reducing infection'
International	'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns to support appropriate antimicrobial use [expert consensus].' 'Establish a new European platform for sharing best practice interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes [expert consensus].' Expand these lines to include campaigns to reduce inappropriate antibiotic use, not just '.. support appropriate AMR use..' and to share best practice (with supporting data on outcomes) on reduction. In Denmark, for example, they have a very well-monitored program to reduce antimicrobial use in agriculture which was able to demonstrate dramatic reductions in use, after changes to the regulations without negative outcomes. That kind of solid data gathering is needed to reassure prescribers that controlling prescription will not harm patients. Modify: 1.' International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns support appropriate antimicrobial use and reduce inappropriate antibiotic use [expert consensus]. 2. Establish a new European platform for sharing best practice (with supporting data on outcomes) interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes [expert consensus].
National and regional	'Fund, develop and implement a national action plan for appropriate use of antimicrobials in human medicine including multi-faceted interventions adapted to local conditions [1] [expert consensus].' Similar to the above, this should be expanded to explicitly include reduction of inappropriate antibiotic use as a goal. Modify: 'Fund, develop and implement a national action plan for the reduction of inappropriate use of antimicrobials in human medicine including multi-faceted interventions adapted to local conditions'

Section of document	Comment and rationale – proposed change
National and regional	'Integrate national antimicrobial stewardship activities into the national antimicrobial resistance plans that include infection prevention and control and vaccination, in a 'One Health' approach [expert consensus].' Vaccines play a key role in preventing the use of antibiotics by reducing (both bacterial and viral) infections, thereby limiting the use of antibiotics (see references.). Guidelines on the prudent use of antimicrobials in human medicines ought to make sure that this preventative intervention is recognised and promoted, not least against the background of the 2014 Council conclusions on vaccination. Add a new bullet saying: 'Improve vaccination coverage in all age groups, through a life-course approach, in order to reduce the use and misuse of antibiotics and in alignment with national plans for the fight against AMR' • Lipsitch M, Siber GR. How Can Vaccines Contribute to Solving the Antimicrobial Resistance Problem? mBio May/June 2016; 7(3): e00428-16. • Cohen, R. (2006). 'Approaches to reduce antibiotic resistance in the community.' Paediatric Infectious Disease Journal 25(10): 977-80. • Dagan, R. and K. P. Klugman (2008). Impact of conjugate pneumococcal vaccines on antibiotic resistance.' The Lancet Infectious Diseases 8(12): 785-95. • Pilishvili, T., C. Lexau, et al. (2010). 'Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine.' Journal of Infectious Diseases 201(1): 32-41. • Coignard et al. (2008). Recent trends in antimicrobial resistance among Streptococcus pneumoniae and Staphylococcus aureus isolates: the French experience'. Eurosurveillance. 13(46): Article 2. • Hampton LM, Farley MM, Schaffner W, et al. Prevention of antibiotic-non susceptible Streptococcus pneumoniae with conjugate vaccines, Journal of Infectious Diseases, 2012, 205, 401–411
National and regional	'Monitor and audit the appropriate use of antimicrobials introducing relevant quality indicators and set up systems for monitoring these indicators. Ensure regular feedback of the results to prescribers [expert consensus].' It would be important to build evidence of vaccination approaches, which have led to a successful impact on AMR, allowing for best practice exchange. 'Monitor and audit the appropriate use of antimicrobials introducing relevant quality indicators, including the effects of vaccination on AMR, and set up systems for monitoring these indicators. Ensure regular feedback of the results to prescribers'.
National and regional	'Supervise and regulate promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing [expert consensus].' Appropriate promotional activities ought to be an essential part of any policy aiming at avoiding misuse of antibiotics. As such, these activities to be very well aligned to appropriate use. Specifically, activities that may lead to increased use should be avoided. However, the most practical and efficient mechanism to do this needs careful consideration, in order to ensure that prescriber/producer interactions remain possible while eliminating inappropriate practices, and we suggest a working group is set up with industry and relevant stakeholders to develop a proposal. Modify: *Set up joint industry and government working groups that develop guidelines on* promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing *while making sure that interactions between producers and prescribers remain possible for information exchange.*
Healthcare facilities	'Documentation in the patient chart of indication, drug choice, dose, route and duration of treatment [expert consensus].' Including the vaccination status in the patient indicators would be important for any program trying to assess the value of vaccination for preventing infections. Without the data being collected on the frontline, it is difficult to get a good grip on the value of potential interventions. Modify: Documentation in the patient chart of indication, drug choice, dose, route and duration of treatment, vaccination status [expert consensus]. Example of indicator: proportion of antimicrobial treatment courses with documentation of indication in the notes, among all antimicrobial treatment courses.
Prescribers	'Prescribers are ultimately responsible for the decision to use, and the choice of, antimicrobials in patient care, and as such need to be provided with appropriate training, guidelines and information in order to be able to exercise prudence in the prescribing of antimicrobials and manage patient expectations' While prescriber training is mentioned in the preamble to this section, it should be emphasized. They ultimately control access to antibiotics in most countries, and they need to feel a personal stake in this issue. It's not enough that institutes offer training programs: prescribers (and their professional societies) need to feel that they have an obligation to be educated and proactive on the issue of AMR). Also, in this section, 'prescribers' is used as a synonym for doctors – but pharmacists and nurses (covered, albeit briefly in sections 6 and 7) are also often prescribers and have the same need for training and ownership. Modify: 'Prescribers are ultimately responsible for the decision to use, and the choice of, antimicrobials in patient care, and as such need to be provided with appropriate mandatory and regular training, guidelines and information in order to be able to exercise prudence in the prescribing of antimicrobials and manage patient expectations. Training courses should be constructed with professional societies and include physicians, nurses and pharmacists. They ought to be constructed in a way that guarantees that prescribers understand the need for constant training.'
Prescribers	'consider relevant host factors: age, immune status, renal function, allergies, foreign bodies and risk factors for antimicrobial resistance (e.g. history of recent antimicrobial use, history of recent travel) [expert consensus]' The words 'immune status' should be clarified. Does this mean risk (i.e. immune competence) or vaccination status? As no vaccine is 100% effective, giving vaccination status too much weight could lead to discounting the possibility of an infection Clarify or delete 'immune status'
Infection control practitioners	What does 'infection prevention' mean? Clarify ' infection prevention'
Education	'Ensure that all healthcare professionals are regularly trained on appropriate antimicrobial use [14,46].' Strategies for *reducing* inappropriate antibiotic use' should also be included Add: '..and on strategies for reducing inappropriate antibiotic use'
Education	Vaccination point needs to be expanded Add the importance to promote higher vaccine implementation and coverage for all ages, since it will contribute to control antimicrobial use and resistance
Research	Point missing Add the following: 'promote research in preventive measures and tools that will reduce our dependence on antibiotics, including improved infection control and vaccines against community and hospital acquired infections and viral or parasitic infections'

Section of document	Comment and rationale – proposed change
Pharmaceutical industry	'Ensure that promotional activities are in accordance with the summaries of product characteristics (SPCs) and national guidelines, and that they mention the risks of antimicrobial resistance and inappropriate use [expert consensus]' Promotional activities must be in line with SPC in any case. We believe that companies need to go further than the proposed limits to promotional activities. Companies should consider specific marketing and sales measures that support appropriate and restricted prescription and use of antibiotics by delinking rewards for employees from the volume of the antibiotic that is sold. As a minimum, such financial incentives should be replaced with measures that directly align with stewardship principles Certain practices such as free samples should also be limited. Modify: 'Ensure that promotional activities aim to reduce resistance by ensuring that the right drug is prescribed at the right dose, for the right duration (stewardship) by mentioning the risks of antimicrobial resistance and inappropriate use, by limiting samples beyond current agreed practices, and by ensuring that financial incentives within companies align with the stewardship principles laid out above.'
Hellenic Society of Chemotherapy (Greece)	
	We would like to congratulate the initiative and express our support to this very sensitive issue affecting an important proportion of European countries, as well as ours. We believe this guidance will be an important aid in the management of increasing antimicrobial resistance, particularly through implication of other stakeholders beyond prescribers.
Prescribers	'select an antimicrobial in accordance with available guidelines, at an appropriate dose and for the shortest effective duration [expert consensus]' We suggest to include ' select an antimicrobial among a class not used by the patient in the last three months'
Prescribers	In Hospitals, we suggest to add as elements: 'Enhance timely and adequate source control for surgical infections' 'Discourage using only antimicrobials instead of surgical treatment/without surgical treatment when there is a clear indication for surgical approach'
Nurses	We suggest to add: 'Develop nursing protocols ensuring correct and timely interpretation of medical orders' 'Develop nursing protocols to independently diagnose the patient in sepsis and trigger diagnostic and treatment algorithms'
Pharmaceutical Industry	We suggest to include: 1. 'Provide incentives and infrastructure for monitoring of resistance after launching of new compounds' 2. 'Provide incentives for monitoring off-label use of new antimicrobials'
International Federation of Anthroposophic Doctor´s Associations (IVAA) (Belgium)	
International	Public health is in need for opening new or unconventional strategies to reduce mis- and overprescription of antibiotics, for example the preventive and curative use of Complementary & Alternative Medicine (CAM)/ Integrative Medicine in (IM) strategies. Please add: Develop European evidence-based guidelines on the preventive and curative use of CAM/IM strategies to reduce mis- and overprescription of antibiotics (expert consensus).
Prescribers	Unless antibiotics are strictly necessary, prescribers could consider the use of certain CAM (Complementary and Alternative Medicine) treatments in mild to moderate infectious illness where there is evidence for effectiveness e.g. in respiratory and urinary tract infections. Research data can be found in the EUROCAM paper 'The role of Complementary and Alternative Medicine (CAM) in reducing the problem of antimicrobial resistance' See: http://www.cam-europe.eu/dms/files/Position_Papers/EUROCAM_PositionPaper_CAM_and_AMR_November2015.pdf Add: 'consider the use of certain CAM (Complementary and Alternative Medicine) treatments in mild to moderate infectious illness where there is evidence for effectiveness e.g. in respiratory and urinary tract infections. [52]
Education/academics	Insufficient knowledge regarding the physiology and appropriate management of fever in children often contributes to an increased parental anxiety, inappropriate antipyretic use, and overutilization of medical resources (Chang, Liu, & Huang, 2013; Crocetti, Moghbeli, & Serwint, 2001; Schmitt, 1980). Parental concerns regarding childhood fever can lead to an overuse of healthcare resources as febrile illness in children accounts for approximately 20% of emergency department visits, 30% of office visits, and over 50% of after-hour phone calls to private physicians (Zomorrodi & Attia, 2008). Research shows that multidimensional educational interventions are most effective in improving parental management of fever (Young et al, 2010). This lack of knowledge regarding fever management pertains also to a large group of nurses and doctors. Please add: 'Include training programs for doctors, nurses and parents in the management of feverish infectious diseases, without or with restricted antipyretics and antibiotic prescription [expert consensus].'
Research	Physicians lack an evidence and expertise-based decision-making tool for safe and effective CAM/IM treatments for infectious diseases of humans (alternatives to antibiotics) in order to reduce misprescription and over prescription of antibiotics. This is especially the case for two indications: (1) infectious diseases where antibiotics are not indicated; and (2) infectious diseases where the resistance problem is very large: bacterial urinary tract infections, enteritis and upper respiratory infections. Integrative treatment strategies could be implemented using 'delayed prescription strategies' (as implemented in the the Dutch GP´s guidelines, for example). Please add: 'Promote high quality research on the safety, effects, working mechanisms and (cost-) effectiveness of CAM prevention and treatment strategies of infections [expert consensus].'
Research group 'Health Systems and Policy' Department of Public Health Sciences Karolinska Institute	
International-organisations, agencies	This section misses important elements such as investing in research and development of new antimicrobials and new point-of-care tests. To add the following items: 'Development of standardised surveillance protocols and mechanisms as well as a platform for information sharing.' 'Promote and financially support research and development of new antimicrobials and new point-of-care tests'
National and regional	Mentioning the One Health approach does not seem to align with the scope of this document. How exactly do they propose national antimicrobial stewardship activities should be based on a One Health approach when the entire scope of the document is to provide guidelines for the prudent use of antimicrobials in human medicine only? We agree that the One Health approach has great benefits for safeguarding antimicrobials however it is only mentioned once in this document, and it appears to be rather ambiguous in their exact intentions with mentioning it. To clearly define the One Health concept and its relevance to the proposed guidelines. To make more explicit the One Health approach by mentioning clear examples of cross-sectoral actors in sections 1 (page 2, lines 46-48); section 2 (page 2, lines 66-68) and section 12 (page 6, lines 308-316)

Section of document	Comment and rationale – proposed change
National and regional	'Ensure national clinical guidance is reviewed and revised when there is a significant change in antimicrobial resistance, new evidence on management of infections or at regular intervals (e.g. 2–3 years) [expert consensus].' It is important to revise the national clinical guidance as well as to actively promote their use by intended end-users. It is also important to distinguish between guidelines for in-patients and out-patients. To add: • Guidelines should be made available to all prescribers, accessibility should be ensured, guidelines widely distributed and promoted, particularly among those clinicians who are more 'isolated' in their community practices. Separate guidelines should be made available for in-patients and out-patient settings respectively
National and regional	'Promote the introduction of electronic antimicrobial prescribing systems able to link clinical indication, microbiological and consumption data [expert consensus].' The recommendation could be more specific to avoid that many separate non-compatible systems are used within a country Rephrase it as follows: 'Promote the introduction of nationwide (hospital and community) electronic antimicrobial prescribing systems'…
National and regional	An appropriate disposal of antimicrobials is an important elements that should be included in national guidelines. This is also in line with the One Health holistic perspective that is mentioned in the documents. To add the following item: 'Introduce appropriate disposal systems in the community setting, i.e. various types of take-back programs, and inform the general public on the correct disposal methods for antimicrobial drugs.'
Healthcare facilities	'An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv).' The microbiologist has a key role in the antimicrobial stewardship team in order to facilitate access to local susceptibility data ('Provide facility-specific cumulative susceptibility reports for common bacterial pathogens against antibiotics that are recommended in the guidelines [expert consensus].') To rephrase the item as follows: ` An antimicrobial stewardship team including at least a clinician, a pharmacist and a microbiologist'
Healthcare facilities	'Guidelines for the diagnosis and management of infections. Example of indicator: proportion of prescriptions compliant with guidelines.' To evaluate if '….prescriptions compliant with guidelines' requires a lot of precision in available data sets and is difficult to perform for all diagnoses Add more specificity ….prescriptions for selected diagnoses compliant with guidelines
Healthcare facilities	'Documentation in the patient chart of indication, drug choice, dose, route and duration of treatment [expert consensus]. Example of indicator: proportion of antimicrobial treatment courses with documentation of indication in the notes, among all antimicrobial treatment courses.' If a culture has been made is an important quality check and should be added To add 'microbiological culture' Documentation in the patient chart of indication, microbiological culture, drug choice…….
Healthcare facilities	'An audit of perioperative antimicrobial prophylaxis choice, timing and duration' Why a particular focus on auditing perioperative antimicrobial prophylaxis only? What about other areas? This can remain as it is, just a note to the working group
Prescribers	'avoid antimicrobial treatment when there is evidence of viral infection or of a self-limiting bacterial infection [expert consensus]' A problem in the document is the use of the term antimicrobial when it clearly refers to antibacterials or antibiotics, one example of this is shown here This becomes problematic e.g. when a patient needs HIV treatment, which could be seen as treatment of a viral infection in which HIV drugs should not be avoided. Because of this it would be better to be specific in the document and use the terms specifically (antibacterial treatment or antibiotics, antiviral treatment, antifungal treatment or antiprotozoal treatment respectively or together when appropriate.
Prescribers	'inform the patient about their antimicrobial treatment' Adequate communication between prescribers and patients should be explicitly promoted Rephrase the item as: ` Inform the patient about the reason for their antimicrobial treatment, explain any potentials negative influences such as on the microbiota, side effects and clarify any misconceptions regarding the treatment prescribed'
Pharmacists	The role of pharmacists could be described further To add the following points in addition to what is already mentioned: - Provide reassurance and support to concerned clients when antimicrobials are unnecessary - Promote the use of symptomatic relief medications when appropriate, particularly for viral, self-limiting infections. - Further, be able to refer patients to a physician if the patient seem to require. - Ensure the safe disposal of antimicrobials (this adds on to 'promote returning leftover antimicrobials') - Function as point of advice, e.g. in telephone advice systems. - Educate the patient on appropriate use of antimicrobials; compliance, timing, etc.
Public/patients	The list provided gives key messages rather than guidelines with which national and local authorities can work. Need to be phrased differently, rather as action points for local entities to work on when targeting the public/patients Needs national and local coordination (one cannot expect the general public/patients to simply get informed on their own). Who shall be at the front line to inform them about appropriate antimicrobial use, AMR and adverse reactions; pharmacists, nurses, prescribers, other stakeholders?
Public/patients	'Do not use leftover antimicrobials' Not just not to use leftover antimicrobials, but also to complete their antibiotic course according to the medical prescription and not to share antimicrobials To add the following points in addition to what is already mentioned: • Do not put pressure on the prescriber to prescribe antimicrobials • Dispose of any remaining antimicrobials properly (according to local guidelines)
Research	To add the following points in addition to what is already mentioned: • Promote research and development of new antimicrobials and new ways of using old antimicrobials

Section of document	Comment and rationale – proposed change
Pharmaceutical industry	This is another section where the One Health approach could be more visible. To add at least one item in relation to the pharmaceutical industry's responsibility in ensuring and/or minimizing the environmental impact of their production process. Particularly in relation to disposal of antimicrobial residues in the environment. This environmental aspect should also be considering when importing antimicrobials manufactured elsewhere
Appendix 2	List is very restricted. If to provide indicators the list should be extensive and divided according to the domains, e.g. hospital, community, education, etc. There are several documents and research articles which provide long lists of indicators, why not refer to them?
Contents	The way the document is structured, it is slightly ambiguous to understand at which level (international, national or local) guidelines for points 3-11 actually are.
Abbreviations	Abbreviation AMR is defined once and then never used, nor is it in the list of abbreviations. A general problem in the document is that the term 'antimicrobial' is used in most instances when actually 'antibacterial' or antibiotic would be more appropriate terms as the content clearly relates to antibacterials. We acknowledge that the term Antimicrobial stewardship is more common that Antibiotic stewardship
Louis Bolk Institute (The Netherlands)	
	See also comments by the International Federation of Anthroposophic Doctor's Associations (IVAA) (Belgium)
National and regional	There are major scientific, political and practical challenges with respect to the emerging risk of AMR. Public health cannot only rely on the development of new (generation of) antibiotics, but is in need for opening new or unconventional strategies, like for example CAM/IM alternatives for antibiotics. Preliminary studies have shown that CAM GP practices and hospitals have substantially lower antibiotic prescription and AMR rates compared to conventional practices. However, CAM strategies vary across countries, clinics and medical doctors. In order to offer conventional physicians a safe and effective alternative to antibiotics and to reduce misprescribing and overprescribing of antibiotics broadly, the available practical expertise and scientific knowledge on CAM/IM strategies must be explored and systemized. Please add: Fund, develop and implement a national action plan for appropriate use of CAM/ IM alternatives for antibiotics in human medicine [expert consensus].
Medicines for Europe (formerly EGA) (Belgium)	
General comment	Medicines for Europe members would strongly encourage drafting of EU-wide therapeutic guidelines which would provide healthcare professionals with much needed detailed instructions on which medicines to prescribe for a specific infection, including all treatment details. The guidelines would be a valuable tools that can help healthcare practitioners take the right therapeutic decision in relation to prescribing habits and the principles of antibiotic prophylaxis in surgery. Both therapeutic guidelines and stricter prescription policies should be complemented by rapid on-site diagnostic tools that would help identify the strain of bacterial infection and the antibiotics to which it is resistant or susceptible – therefore allowing more precise prescribing. Moreover, current national-centric approach brings much confusion to patients who are subject to health systems in different countries and might divert from adherence to the prescribed antimicrobial treatment. A harmonised approach could have additional collateral benefits in terms of pack sizes available on different markets. Namely, at the moment different member states opt for different solutions and preferences, which push the pharmaceutical companies to rethink which pack sizes make a sustainable business decision, which might lead to shortages of these essential medicines.
General comment	Raising awareness of antimicrobial resistance and education of all stakeholders involved is critical to tackling this issue. Responsibility and role in empowering patients should be clearer and well defined. There is still a big difference among countries and a tailored plan how governments are/will tackle this threat should be guided from EU and global perspective.
Introduction	'The exposure of microorganisms to antimicrobial agents creates the selective pressure that leads to the development of resistance' Exposure of micro-organisms to antimicrobial agents is not the only form of selective pressure that selects for resistance to antimicrobials. The best example is the induction of efflux pumps by conditions other than drug exposure. 'The' should be changed to 'a' since we know of examples of resistance mechanisms that are selected for in the absence of exogenous antimicrobial pressure, but which nevertheless result in shifts in antimicrobial susceptibility. 'The exposure of microorganisms to antimicrobial agents creates a selective pressure that leads to the development of resistance.'
International	As antimicrobial resistance does not respect borders, we fully support the section dedicated to 'International – organisations and agencies'. We would welcome further elaboration of the definition of the target audience of this section by referencing organisations and countries, both inside and outside the EU. 1. Amend the title: 'International – governments, organisations, agencies' 'International cross-sectoral, inter-organisational collaboration and coordination is required to establish ..' 2. Amend text to read: 'International cross-sectoral, inter-organisational and government collaboration and coordination both within and outside the EU is required to establish'
International	'Ensure access to essential antimicrobials by supporting market availability' This can be read to apply both to uptake of novel antimicrobials and sustained availability of existing antimicrobials. Explicitly including both innovative products and essential generic antimicrobials in this principle would be helpful, as the support and interventions needed for market availability will differ for innovative vs. generic products. 1. Amend to read: 'Ensure access to essential antimicrobials by supporting market availability for both innovative and generic products' Furthermore, while global access to essential antimicrobials is a key goal, this should also be reflected in the section pertaining to national and regional governments, administrators and public health agencies. International organisations and agencies have an important role to play in setting global standards, but the availability of any given product will depend on the market conditions of a particular country. As health remains a national competency, country-specific barriers to market availability will need to be addressed independently of action by international organisations. 2. Insert new text in Section 2. 'National and regional to read: 'Ensure access to essential antimicrobials by conducting a review of national market availability and by implementing measures to support sustained market availability for both innovative and generic products'

Section of document	Comment and rationale – proposed change
International	'Establish a list of antimicrobials with restrictive measures for use' Any measures to restrict use of antimicrobials should consider the balance of this goal with the need for sustained market availability of products that continue to be necessary, albeit in lower quantities. In this regard, restrictions should not be placed in a way that impacts generic competition and supply availability. Decision-making for any such list should be based on scientific evidence in a risk-based approach, and input from all stakeholders including the pharmaceutical industry should be taken into consideration. Amend existing text in Section 2. 'National and regional' to read: 'establish a list of antimicrobials with restrictive measures for use, considering market availability of essential products'
National and regional	Antibiotics should be available upon prescription only. Ensure that antimicrobials are available upon prescription only, are consumed only by the patient for whom they are prescribed, and that the unused balance is appropriately destroyed or returned to the prescriber or pharmacy.
National and regional	It is of essence to make sure all healthcare professionals who prescribe antibiotics (e.g. nurses, dentists) should be educated about the risks of antimicrobial resistance, and made aware of the applicable guidelines. Define which categories of healthcare professionals should be in a position to prescribe.
National and regional	'Explore per unit dispensing of antimicrobials to match pack size with planned course duration according to national guidelines [expert consensus].' We are aware of some attempts of per-unit dispensing, e.g. current pilot in France, or through dose dispensing services in which patients receive blister packs containing medicines in line with the planned course duration as prescribed, as commonly done already in some countries such as the Netherlands. Per-unit dispensing should be considered in view of the significant legal, regulatory and practical implications in terms of Good Distribution Practices, Good Manufacturing Practice, implementation of the Falsified Medicines Directive (traceability, risks of counterfeited medicines), etc. Additionally, per unit dispensing could create a number of technical challenges at pharmacy and hospital level (lack of technical infrastructure/governance/capabilities for a proper per unit dispensing), which should also be considered. The proposal should be also reviewed from the national reimbursement systems perspective, which often limit the possibility of per-unit dispensing. Amend existing text to read: 'Explore with caution per unit dispensing of antimicrobials to match pack size with planned course duration according to national guidelines, taking into consideration all relevant guidelines and regulations, as well as market availability of essential products and prescriber's choice.'
National and regional	'Supervise and regulate promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing [expert consensus].' Promotional activities are already strictly regulated, thus making sure that they are strictly limited to the Summary of Product Characteristics (SPC) of a medicine. It is in everyone's common interest to ensure appropriate use, and pharmaceutical industry is already actively engaged in contributing to appropriate antimicrobial prescribing. In addition to the existing EU and national framework, the EU research-based pharmaceutical industry (EFPIA) and the generic industry (Medicines for Europe) have established codes regulating promotional activities and interactions with healthcare stakeholders. Link to the code of conduct: http://www.medicinesforeurope.com/medicines-for-europe/#section-7 We also caution against taking a broad interpretation of this principle. Restriction on the ability of pharmaceutical companies to engage in antimicrobial awareness campaigns or other educational activity pertaining to AMR would limit the collective effort to promote prudent use of antimicrobials. Amend existing text to read: 'Continue supervision and regulation of promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing.'
Healthcare facilities	'A policy for preauthorisation and/or post-prescription review' We note with caution that preauthorisation could lead to inadvertent delay in appropriate patient care in an emergency setting. Implementation of this principle will require careful consideration of risk/benefit for patient care.
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment' We fully support this principle, and would welcome encouragement through these guidelines for development and widespread availability of rapid point-of-care diagnostics to help prescribers identify bacterial as opposed to viral infection, particularly in primary care settings.
Healthcare facilities	'Ensure timely access to clinical microbiology laboratory services. For acute care hospitals, these services should be provided on a 24/7 basis for critical specimens [expert consensus].' This would require large investments in resources and FTEs to be able to provide 24/7 clinical microbiology staff and access to testing equipment. In addition these tests are often batched, so having rapid turnaround for all patient susceptibility testing would be an immense burden on a facility. Please delete
Prescribers	Prescribers should give clear instructions on how to take the treatment and inform patients about the risk of antimicrobial resistance associated with the inappropriate use of antibiotics. In some cases, the patient is not able to comprehend the information (age, mental status, physical condition). Information should be directed at patient and/or responsible caregiver. Prescribers should inform the patient about their antimicrobial treatment, and that they or the responsible caregiver should notify the physician if they are unable to comply with the doctor's therapeutic decision.
Prescribers	'in high-risk patients, avoid the use of antimicrobials that are associated with increased risk for *Clostridium difficile* infection if there are alternatives [14,20,45]. Example of indicator: incidence of *Clostridium difficile* infections' If a patient is at high risk for CDI, there is a low probability that changing from an antibiotic associated with increased risk for CDI to one associated with lower risk is going to be a successful strategy. These patients already have altered flora due to prior antibiotic use and/or increased exposure to *C. difficile* spores because they are institutionalized and/or have altered immune statuses due to underlying conditions or age. It's not clear that association of a drug with CDI should be a driver of choice of antibiotic in a population that is already at high risk for CDI, as those patients will likely experience a bout of CDI regardless of whether the antibiotic they are prescribed is considered of higher or lower risk of inciting CDI in an otherwise low-risk population. Please delete

Section of document	Comment and rationale – proposed change
Pharmacists	'Do not dispense antimicrobials without prescription, unless specific provisions allow for regulated dispensation in specific circumstances [expert consensus]' As a principle, antibiotics should be available upon prescription only. Any exceptions should be clearly defined (eg. Public health threats). Do not dispense antimicrobials without prescription, unless specific provisions allow for regulated dispensation in extraordinary circumstances.
Public/patients	The role of the public/patients in addressing AMR is critical, and we believe this section could be expanded to identify ways to ensure the public/patients are fully aware of the implications of AMR and their role in prevention – both in taking preventive action to avoid infection (hand-washing, vaccination) and in preventing AMR though proper antimicrobial treatment completion. A shift in mind-set is needed in many countries to encourage patient questioning of need for instead of requesting antibiotic prescription. Insert new text to read: 'Complete each antimicrobial treatment course as prescribed 'Practice infection prevention through proper sanitisation and regular vaccination, as recommended by guidelines'
Research	'Research the risk of specific antimicrobials and antimicrobial classes for the selection of antimicrobial resistance in microbiota to allow ranking and rational use [expert consensus]' The word 'ranking' is not clear/confusing. In order to thoroughly study the risk of selecting for resistance among the microbiota one would need to have a means to culture the entire microbiota, and correlate levels of in vitro susceptibility with clinical outcomes. This is not a practical approach to ranking the selection of which drugs should be prescribed over which others. Please delete
Research	'Promote research on rapid and point-of-care diagnostics to support evidence-based guidelines for the role of diagnostics in appropriate antimicrobial prescribing [expert consensus].' The bottleneck is in diagnostic development, clinical testing, and implementation in clinical microbiology laboratories. It is not only in research. Modify: Promote research, development, commercialization and implementation of rapid and point-of-care diagnostics to support evidence-based guidelines for the role of diagnostics in appropriate antimicrobial prescribing
Pharmaceutical industry	'Ensure that promotional activities are in accordance with the summaries of product characteristics (SPCs) and national guidelines, and that they mention the risks of antimicrobial resistance and inappropriate use [expert consensus]' Promotional activities are already strictly regulated, thus making sure that they are strictly limited to the Summary of Product Characteristics (SPC) of a medicine. In addition to the existing EU and national framework, the EU research-based pharmaceutical industry (EFPIA) and the generic industry (Medicines for Europe) have established codes regulating promotional activities and interactions with healthcare stakeholders. Delete: Ensure that promotional activities are in accordance with the summaries of product characteristics (SPCs) and national guidelines Link to the code of conduct: http://www.medicinesforeurope.com/medicines-for-europe/#section-7
Pharmaceutical industry	'Adapt pack size and strength to indications [14] [expert consensus]' While agreeing with the rationale behind this principle in light of the considerable misuse of antimicrobials due to lack of compliance with full treatment course and subsequent self-medication with leftover treatment, the introduction by manufacturers of pack size matched with course duration will require careful consideration of market mechanisms to ensure sustainability and competition. Course duration may vary for the same product based on different medical situations, potentially creating a complicated regulatory, procurement and distribution situation if a broad spectrum of pack sizes is required. Additionally, limitations on pack size availability could interfere with prescribers exercising professional judgement in treatment course duration to meet patient needs. Patient's consumption of a given number of units (e.g. tablets) of antibiotics shouldn't depend on package size but on doctor's ordinance (via prescription). Industry is not in a position to predict all potential therapeutic schemes which could be prescribed by doctors in each individual case, and adjust upfront packages of all units as well as the strength of the active substances. Due to the above mentioned difficulties, the technical feasibility of implementation of such a change is very low. If there are any units (e.g. tablets) remaining at the end of the treatment course, we would recommend empowering pharmacists to explain to patients how to properly disposed of remaining antibiotics, in line with national provisions. (as provided under point 6.b – lines 247/248). Please note that the industry is already engaged in so called medsdisposal campaign: http://medsdisposal.eu/ The proposal should be also reviewed in light of antibiotics dispensed in hospital settings (e.g. surgery) where patients are not in contact with antibiotic packages (and would not be able to notice any additional warning information). Such a proposal would lead to the creation of a significant number of different packages and strengths of the active substances, which could increase the risk of drug shortages in the antibiotics area, thus putting patients' health at risk. Changing packages and the strength of the active substance might have legal and regulatory implications, since this may require manufacturers to conduct new clinical trials, and request new marketing authorizations, etc., which represent a high burden for the manufacturers. This type of proposal should be subject to a thorough impact assessment evaluating the legal (pharmaceutical regulatory framework), economic and public health implications, before being further discussed. In conclusion, this proposal may have unintended consequences, and the cost of the proposed adjustment could be disproportionally significant vs. the potential healthcare benefits. Delete recommendation

Section of document	Comment and rationale – proposed change
Pharmaceutical industry	'Consider special labelling of antimicrobial packages that identify them as such and indicate that they are medical products for specific use only as prescribed [expert consensus]' In principle, antibiotics should be available upon prescription only and the additional labelling of packages will not influence doctors' therapeutic decision regarding the number of units being prescribed (e.g. tablets). The proposal should be also reviewed in light of antibiotics dispensed in hospital settings (e.g. surgery) where patients are not in contact with antibiotic packages (and would not be able to notice any additional warning information). Prescribers should give clear instructions on how to take the treatment and inform patients about the risk of antimicrobial resistance associated with the inappropriate use of antibiotics. Alternatively, one may consider including in the Summary of Product Characteristics (SPC) and/or the Patient Information Leaflet (PIL) relevant information related to AMR e.g. 'Prescribing xxx in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria' (FDA example). Changing the outer packaging would lead to unnecessary burden on industry and regulators side when implementing the changes, which could be much more easily and efficiently addressed by education and proper dialogue among healthcare professionals and patients. Change of the wording to: 'Consider including in the Summary of Product Characteristics (SPC) and/or the Patient Information Leaflet (PIL) relevant information related to AMR e.g. *Prescribing xxx in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria*.
MedTech Europe (Belgium)	
Definitions	**'**Antimicrobial stewardship programmes refer to a coordinated programmes that implement interventions to ensure appropriate antimicrobial prescribing and effective antimicrobial treatment, to limit antimicrobial resistance and to prevent *Clostridium difficile* infections' The holistic approach- from prevention to treatment- of the stewardship programmes should be specified. Modify: '…ensure prevention, appropriate diagnosis and antimicrobial prescribing and…' Broaden the scope of antimicrobial stewardship programmes to ensure maximum prevention of infections by not specifying C.Diff. Modify: 'and to prevent infections.'
Definition	Add definition of 'healthcare acquired infections' (HAI) as infection control is also referred to in the Guidelines & highlighted by ECDC as an overlapping subject. Explain the relation with AMR. HAIs are infections caused by a wide variety of bacteria, fungi, and viruses during the course of receiving medical care. The issues of AMR and HAI overlap widely, but are not synonymous- many of the HAIs are also resistant to antibiotics. Prevention of HAIs helps preventing AMR after medical treatment.
International –	'Develop European evidence-based guidelines on the use of rapid and point-of-care diagnostics [expert consensus].' Mention implementation as well, to ensure continuity in the process. Modify: 'Develop and facilitate implementation at Member State level of European evidence-based guidelines…'
National and regional	Add special focus on prescribers. Add: 'Develop and implement funding schemes for GPs and other relevant prescribers at national level. Eg.Right diagnosis/testing when possible should prevail the prescription of antibiotics.'
Healthcare facilities	Add another section on available technologies, which will help the professionals to prioritise and be aware of available alternatives and tests. Add: 'Continuously updated list of available/new antibiotics, diagnostic tests, medical devices and other alternatives for infection prevention and control.'
Prescribers	Add another section on overall infection prevention in hospitals before going into detail. E.g. Follow the WHO surgical safety checklist to avoid development of infections.
Pharmacists	'Pharmacists are the gatekeepers to the use of antimicrobials and can act as an important source of advice and information for patients, and as such need to be provided with appropriate training, guidelines and information in order to be able to exercise prudence in the prescribing of antimicrobials and manage patient expectations...' Hospital pharmacists are often buyers of not only medicines but also diagnostic tests and medical devices, both of which can help prevent the development of resistance. Modify: 'to the use of antimicrobials as well as to diagnostics and medical devices that help preventing resistance, and can act as an important…' Modify '…prudence in the prescribing of antimicrobials, use of diagnostic tests and medical devices and manage patient expectations.'
Nurses	'The role of nurses within the clinical team, and in particular their regular contact with patients and their role in administering medicines, can be critical to ensuring that antimicrobials are taken according to the prescription and for monitoring the response to antimicrobials (including potential adverse effects).' Diagnostic tests and medical devices also play a large part in prevention of over and misuse of antimicrobials and therefore we suggest including them in the scope of the nurses' responsibilities. 1. Modify: '…that antimicrobials as well as the use of diagnostic tests and medical devices are taken according to the prescription and their intended use respectively…' Suggest implementing supporting technologies for monitoring. 2. Modify: '…monitoring the response to antimicrobials, for example through electronic surveillance systems.'
Education/academics	Add a section on training on existing guidelines that contribute to infection reduction. Add: 'Introduce trainings on WHO Surgical safety checklist and WHO guidelines on hand hygiene in healthcare.'
Research	'Promote research on rapid and point-of-care diagnostics to support evidence-based guidelines for the role of diagnostics in appropriate antimicrobial prescribing' Medical devices also play a great role in preventing resistance, therefore it should be included next to diagnostic tests. Modify: '…point of care diagnostics and medical devices to support…for the role of innovative technologies in appropriate antimicrobial prescribing and infection prevention.'
Research	Add a line ensuring access to new technologies. Add: 'Ensure access and uptake of new technologies through appropriate funding systems.'
Add: Medical technology industry	Given the large role the medical technology plays in preventing the misuse and overuse of antibiotics and preventing infections, we would recommend to add a section on specific recommendations for our industry based on expert opinions. MedTech Europe would be available for further discussions on this, if needed.
Ministry of Health also on behalf of the National Institute for Public Health and the Environment (RIVM) and the Dutch Working Party on Antibiotic Policy (SWAB)	

Section of document	Comment and rationale – proposed change
Authors/acknowledgements	There seems to be little room in the process for policy officers/government authorities to get involved. The document is partly meant for the target group government authorities – therefore involve policy makers in drafting instead of using only expert group and expert level
Authors/acknowledgements	Unclear how this draft report will change because of comments public consultation and stakeholder meeting on 16th of September We would like to see a revised document before 31st of October
Introduction	Important context as presented at 1st stakeholder meeting is missing: the EU guidelines are part of the Council conclusions on AMR adopted at the Health Council on the 17th of June 2016. Mention that EU Member States requested these EU guidelines - as stated in the council conclusions
Definitions	Do not use own definitions that cause discussion, because these already defined elsewhere Refer to existing definitions e.g. EMA
Purpose	Unclear who is target audience of document – and this is reflected throughout the whole document; structure is missing Make clear that the document is targeting 2 groups; 1) professionals 2) and governments and apply structure in the whole document (use these separate subheadings in each paragraph, e.g. mention long term goals under heading governments and short term treatment options for patients under the heading professionals)
Scope	The scope is not precise: The statement that the report will not cover specific medical conditions or specific antimicrobials is not in line with certain recommendations As examples, recommendation 5.a.i. is very specific. Idem 5.c.ii. and 5.c.v. These are very important principles in the treatment of individual patients and have great influence on morbidity (like adverse drug events) and mortaliy; but no impact on development of resistance. Throughout the document, there should be made clear if a measure targets outcomes at a patient-level (ADE's, mortality) or outcomes at a society-level (costs, resistance)
Principles and elements for inclusion in guidelines	This section feels like top-down prescribing HOW member states should act We suggest to follow structure as used in the EU veterinary guidelines on prudent use of antibiotics; general principles were stated (WHAT should be done ; e.g. you need to have national guidelines in place) followed by suggestions to member states HOW this could be done for each target group (e.g. minimal requirements as agreed upon scientifically in these guidelines are ...).
Principles and elements for inclusion in guidelines	Many measures are mentioned – however we would prefer to mention a limited number of measures that are truly beneficial We suggest starting with situations in which you do NOT need to use antibiotics (this is how we were able to reduce ab use in the veterinary domain in NL). The next phase is mentioning conditions to be met if you do need to use antibiotics
Principles and elements for inclusion in guidelines	We are happy to see that the content of this section generally corresponds to what we are doing in NL
Principles and elements for inclusion in guidelines	Enforcement is missing/or somewhat hidden in the document As mentioned during the first stakeholder meeting, enforcement of rules and guidelines on prudent use is a very important aspect and should be mentioned as a specific minimal requirement for government authorities.
Pharmacists	It seems to be suggested that pharmacists are responsible for prudent use of antibiotics – but this is a shared responsibility of professionals Make clear that the role of pharmacists in ensuring prudent use of antibiotics – is to make sure antibiotics are not distributed to patients without a doctor's prescription.
References	The recent O'Neill report is not used Add very nicely structured conclusions and next steps from the O'Neill report in the document
Appendix 2	This list seems to be assembled quickly and not evidence-based. It is not acceptable for publishing in this way. We suggest to not include an appendix with indicators in this document at this stage. Instead, make a decent study of indicators after reaching consensus on the EU guidelines. It should be made clear if indicators should measure the effectiveness of strategies and interventions implemented or if they should measure clinical outcomes. For this, scope needs to be defined, strategies targeting the scope chosen, and objectives linked to outcomes. Only then, useful indicators can be chosen. Based on experience in the NL we have strong objections to some of the indicators mentioned and provide recommendations for improvement and more appropriate indicator in the rows below.
Appendix 2	'Proportion of prescriptions compliant with guidelines' Measuring this indicator is very time-consuming, and in addition in many cases it can be valid NOT to follow the guideline As a first step, as structure indicator might be more reasonable: 'A current local antibiotic guideline should be present in the hospital, and an update should be done every 3 years' (van den Bosch CM, et al. Quality indicators to measure appropriate antibiotic use in hospitalized adults. Clin Infect Dis. 2015;60:281-91). As an alternative, the indicator could be: provide a list of antibiotics prescribed for certain infections (CAP, UTI). This will give insight in prescribing practices, without the need to judge on a case-by-case basis whether deviation from the guideline was justified. This could be applicable to primary care, hospitals and long-term care facilities.
Appendix 2	Missing indicator A policy for pre-authorisation and/or post-prescription review. We think this would also be a perfect structure indicator, and, in a second stage, reporting the proportion of justified prescriptions of restricted antibiotics could be feasible. This is an activity most stewardship teams perform (or should perform), and should be able to report on.
Appendix 2	'Proportion of combination treatments among total number of antimicrobial treatments' Use of combination therapy can be justified in some cases and not in others. This requires assessment on a case-by-case basis. This will be very time-consuming, and we fear the level of agreement between experts (Kappa) might be low, rendering this not a useful indicator. Remove indicator
Appendix 2	Missing indicator Section 5 summarizes the actions/behavior expected from prescribers. A recent systematic review and meta-analysis revealed that several stewardship objectives can lead to significant benefits for clinical outcome, adverse events, costs and bacterial resistance rates in hospitals (reference 7). Most of these are included in this guideline, but 'Bedside consultation in case of *S. aureus* bacteremia is not included in this section, while several studies have shown that this leads to increased survival. We suggest to add this as an indicator.
MSD Europe Inc. (Belgium)	

Section of document	Comment and rationale – proposed change
General	MSD fully supports the publication of a European-wide guideline on the appropriate use of antimicrobials based on the ECDC's draft technical report. As a manufacturer of antibiotics we support all efforts designed to ensure that these critical medicines are used only when and where appropriate, thereby helping to guarantee the future availability, supply and effectiveness of effective treatments worldwide. Areas where the company feels the guideline could be improved have been included herein.
Introduction	'Inappropriate use of antimicrobials accelerates the emergence and dissemination of resistance' All usage of antimicrobials drives resistance. It is suggested that this line be clarified to make it clear that inappropriate usage is the 'modifiable factor' that the various actors referenced within the document can help to control. MSD would suggest amending the line to read: All usage of antimicrobials contributes towards the emergence and dissemination of resistance, however inappropriate use of antimicrobials can serve to accelerate this process – a modifiable factor that we can hope to decrease or eliminate.
International	'International collaboration in designing, implementing and monitoring antimicrobial stewardship interventions and campaigns to support appropriate antimicrobial use [expert consensus].' It is suggested that this line be modified to distinguish between what is appropriately handled at the international level (the sharing of intelligence, surveillance data and best practice strategies), as opposed to the national level (design and implementation). MSD would suggest amending the line to read: International collaboration in monitoring antimicrobial stewardship interventions and the active sharing of national design and implementation strategies and campaigns to support appropriate antimicrobial use
National and regional	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7].' Restriction can be an effective means to help control an outbreak of resistance; however MSD would query the need to include this as a required element of the ECDC guideline. If inclusion is deemed necessary then the recommendation could be strengthened by including clarification on where and when this may be appropriate.
National and regional	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8]' MSD would suggest clarification of this line to reference 'education' specifically. National campaigns for antibiotic use should also be supported by national campaigns for increased vaccination uptake. Publicly linking increased vaccination with reductions in antibiotic usage and resistance would send a strong message to the public. MSD would suggest adding the following: Fund, design, implement and assess national educational campaigns on antimicrobial use and vaccination targeting the public and health professionals
National and regional	'Supervise and regulate promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing [expert consensus].' The terms 'supervise' and 'regulate' within the context of an appropriate-use guideline risk implying occurrences of inappropriate behaviour on the part of manufacturers. Moreover, as currently worded, this paragraph could also imply that regulations are not currently tough enough in some jurisdictions and require amending. The industry as a whole is in fact one of the most regulated industries in Europe with strict rules governing behaviour and sales activity. Therefore, with a view to minimising the risk of misinterpretation, MSD would ask that a revision to this paragraph be considered. MSD would suggest amending the paragraph to read: Work with the pharmaceutical industry to ensure that promotional activity contributes to, and educates healthcare professionals on, appropriate antimicrobial prescribing
Healthcare facilities	To account for international efforts to tackle antimicrobial resistance, MSD would suggest that consideration should be given to the alignment of this section with the 7 core elements of hospital stewardship programmes promoted by the U.S. Centres for Disease Control and Prevention (in so far as is possible)
Prescribers	Given the prescriptive nature of some of the recommendations contained within section 5 and the fact that some of the desired actions span multiple disciplines, particularly pharmacy, it is suggested that clarification be provided so as to make it clear that the recommendations span professions. Currently the sections relating specifically to pharmacists, nurses and infection control practitioners look under-developed by comparison.
Research	Consideration should be given by the ECDC to expand this section on research recommendations to include reference to: • Risk stratification of patients • Real world outcomes research Use of electronic clinical decision support
Pharmaceutical Industry	'Ensure that promotional activities are in accordance with the summaries of product characteristics (SPCs) and national guidelines, and that they mention the risks of antimicrobial resistance and inappropriate use [expert consensus]' We agree that the pharmaceutical industry is a key partner to ensure the prudent use of antimicrobials, but have several questions and comments regarding this section. Please provide clarity on the intent of this point. As written, the interpretation, feasibility and practical applications are unclear. First and most importantly, we note that promotional activities are regulated and strictly limited to the information contained with the drug label. National, local and institutional guidelines may differ from a product's labelling for a variety of reasons. As such, sponsors could not agree to a broad recommendation to ensure that promotional activities are accordance with national guidelines. Second, we note some potential limitations of guidelines (national, local and instructional) with respect to this broad recommendation, including the lack of guidelines for new antibiotics and the frequency of updating the recommendations. Furthermore, it is also worth recognizing that the level of scientific evidence underpinning recommendations in guidelines is variable. Finally, given regulations regarding promotion, labels would presumably have to include language to support mentioning the risks of antimicrobial resistance and inappropriate use. A general statement such as the following could serve this purpose: 'To reduce the development of drug-resistant bacteria and maintain the effectiveness of [Trade name] and other antibacterial drugs, [Trade name] should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.' Since regulations generally dictate the content of drug labels, a requirement for such a statement would have to come from the regulators, and not necessarily a drug sponsor. Modify: Ensure that promotional activities are in accordance with the summaries of product characteristics (SPCs), and that they mention the risks of antimicrobial resistance and inappropriate use
	'Adapt pack size and strength to indications [14] [expert consensus]' We are concerned about this broad recommendation and the feasibility of adapting pack sizes to indications given that specific drugs may be approved for multiple indications, strengths and formulations. Such decisions are multi-factorial, made on a case-by-case basis, and include discussions with regulators. We respectfully request the removal of line 314

Section of document	Comment and rationale – proposed change
Pharmaceutical Industry	Suggested new sub-paragraphs to further underpin the statement made in line 308 in respect to the industry as a 'key partner'. MSD would suggest adding the following sub-paragraphs: 1. 'Encourage, when conducting promotional activities (and where relevant, appropriate and permitted) the adoption of diagnostic technologies that are designed to facilitate faster diagnosis and identification of optimal treatment regimens' 2. 'When engaging with payers and prescribers, aid (where appropriate, relevant and permitted), the dissemination of educational materials produced by national public health agencies' 3. 'Encourage internal company awareness of antimicrobial resistance, particularly across divisions and functions that may not be directly related to the research, development or commercialisation of antimicrobials' 4. 'Engage with national and international policy-makers to support the development of policies that promote appropriate antimicrobial prescribing, including the design of novel reimbursement systems and processes that may help to aid appropriate access to antimicrobials'
Vaccine Specific Points	'Set qualitative and quantitative targets for improvement of prescribing [expert consensus]. Example: antibiotic quality premium (NHS England) [2].' Setting qualitative and quantitative use for antibiotics should also be supported by improvement of practice and performance in vaccination uptake and coverage rates which have been demonstrated to reduce antibiotic use. MSD would suggest amending the line to read: Set qualitative and quantitative targets for improvement of antibiotic prescribing and vaccination coverage.
Vaccine Specific Points	'Ensure availability of national clinical guidance based on antimicrobial resistance patterns for the community, long-term care facilities and hospitals [3,4] [expert consensus].' National clinical guidelines should include recommendation of vaccination to reduce antibiotic use. MSD would suggest amending the line to read: Ensure availability of national clinical guidance based on antimicrobial resistance patterns and vaccination coverage for the community, long-term care facilities and hospitals
Vaccine Specific Points	'Explore incentive systems for appropriate prescribing [expert consensus] [9]' To take a systems approach to reduce antimicrobial resistance it would be wise to explore both incentive systems for appropriate antibiotic prescribing and the potential increased role of vaccines. MSD would suggest amending the line to read:Explore incentive systems for appropriate antibiotic prescribing and vaccine uptake
Vaccine Specific Points	'Explore motivational and system change approaches to optimise antimicrobial prescribing.' Motivational changes are arguably of equal importance in increasing coverage of vaccines. MSD would suggest amending the line to read: Explore motivational and system change approaches to optimise antimicrobial prescribing and the increased uptake of vaccines
Vaccine Specific Points	'consider relevant host factors: age, immune status, renal function, allergies, foreign bodies and risk factors for antimicrobial resistance (e.g. history of recent antimicrobial use, history of recent travel) [expert consensus]' Vaccination status could also be a risk/protective factor that could be documented. MSD would suggest amending the line to read:consider relevant host factors: age, vaccination status, immune status, renal function, allergies, foreign bodies and risk factors for antimicrobial resistance (e.g. history of recent antimicrobial use, history of recent travel)
Vaccine Specific Points	MSD would ask that consideration be given to the addition of a reference to vaccination in the community – which if encouraged, could aid in reducing demand for antibiotics over time. MSD would suggest adding a new sub-clause for 'In the community' to read: uptake of vaccines should be encouraged by healthcare professionals in the community to reduce illness and subsequent antimicrobial use
Vaccine Specific Points	Both nurses and pharmacists play an important part in vaccinating adults and educating patients about vaccination. This should be reflected in the text.
Vaccine Specific Points	It is important to highlight to the public and healthcare professionals the link between vaccinations and the associated impact on antibiotic use. As such this section should specifically mention the need for education in this area. MSD would suggest adding an additional line that reads: Ask a healthcare professional for advice on vaccinations you may be eligible to receive, which if administered, may reduce both your risk of developing an illness and the need for future antibiotic treatment.
Mylan (Belgium)	
International	As antimicrobial resistance does not respect borders, we fully support the section dedicated to 'International – organisations and agencies'. We would welcome further elaboration of the definition of the target audience of this section by referencing organisations and countries, both inside and outside the EU. 1. Amend title to read: 'International – governments, organisations, agencies' 'International cross-sectoral and inter-organisational collaboration and coordination is required to establish standards, systems and procedures necessary to control and prevent the cross-border spread of antimicrobial resistance and to ensure the sharing of best practice and support capacity development' 2. Amend text to read: 'International cross-sectoral, inter-organisational and government collaboration and coordination both within and outside the EU is required to establish'
International	'Ensure access to essential antimicrobials by supporting market availability' This can be read to apply both to uptake of novel antimicrobials and sustained availability of existing antimicrobials. Explicitly including both innovative products and essential generic antimicrobials in this principle would be helpful, as the support and interventions needed for market availability will differ for innovative vs. generic products. Furthermore, while global access to essential antimicrobials is a key goal, this should also be reflected in the section pertaining to national and regional governments, administrators and public health agencies. International organisations and agencies have an important role to play in setting global standards, but the availability of any given product will depend on the market conditions of a particular country. As health remains a national competency, country-specific barriers to market availability will need to be addressed independently of action by international organisations. 1. Amend text to read: 'Ensure access to essential antimicrobials by supporting market availability <u>for both innovative and generic products</u>' 2. Insert new text in Section 2. 'National and regional' to read: '<u>Ensure access to essential antimicrobials by conducting a review of national market availability and by implementing measures to support sustained market availability for both innovative and generic products</u>'

Section of document	Comment and rationale – proposed change
International	'Establish a list of antimicrobials with restrictive measures for use' Any measures to restrict use of antimicrobials should consider the balance of this goal with the need for sustained market availability of products that continue to be necessary, albeit in lower quantities. In this regard, restrictions should not be placed in a way that impacts generic competition and supply availability. Decision-making for any such list should be based on scientific evidence in a risk-based approach, and input from all stakeholders including the pharmaceutical industry should be taken into consideration. Amend existing text in Section 2. 'National and regional' to read: 'establish a list of antimicrobials with restrictive measures for use, considering market availability of essential products'
National and regional And Pharmaceutical industry	'Explore per unit dispensing of antimicrobials to match pack size with planned course duration according to national guidelines' 'Adapt pack size and strength to indications' While agreeing with the rationale behind this principle in light of the considerable misuse of antimicrobials due to lack of compliance with full treatment course and subsequent self-medication with leftover treatment, the introduction by manufacturers of pack size matched with course duration will require careful consideration of market mechanisms to ensure sustainability and competition. Course duration may vary for the same product based on different medical situations, potentially creating a complicated regulatory, procurement and distribution situation if a broad spectrum of pack sizes is required. Additionally, limitations on pack size availability could interfere with prescribers exercising professional judgement in treatment course duration to meet patient needs. Manufacturer adaptation of strength to match indications could be explored, noting that the dose strength of an antibiotic has an implication on the antimicrobial resistance level as a higher dose can overcome resistance by exceeding the Minimum Inhibitory Concentration (MIC). Unit dispensing at pharmacy level could be a more viable solution, either by cutting existing packs to match the prescribed units as is currently being piloted in France, or through dose dispensing services in which patients receive blister packs containing medicines in line with the planned course duration as prescribed, as commonly done already in some countries such as the Netherlands. At national level 1. Amend existing text to read: 'Explore per unit dispensing of antimicrobials to match pack size with planned course duration according to national guidelines, taking into consideration market availability of essential products and prescriber choice.' At Pharmaceutical Industry level 2. Amend existing text to read: 'Explore adaptation of pack size and strength to indications'
National and regional –	'Supervise and regulate promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing' While we fully support the need to ensure promotional activities do not interfere with appropriate antimicrobial prescribing, we note that supervision and regulation of promotional activity by the pharmaceutical industry is already in place. It is in everyone's common interest to ensure appropriate use, and pharmaceutical industry is already actively engaged in contributing to appropriate antimicrobial prescribing. We also caution against taking a broad interpretation of this principle. Restriction on the ability of pharmaceutical companies to engage in antimicrobial awareness campaigns or other educational activity pertaining to AMR would limit the collective effort to promote prudent use of antimicrobials. Amend existing text to read: 'Continue supervision and regulation of promotional activity by the pharmaceutical industry, so it contributes to appropriate antimicrobial prescribing.'
Healthcare facilities	'A policy for preauthorisation and/or post-prescription review' We note with caution that preauthorisation could lead to inadvertent delay in appropriate patient care in an emergency setting. Implementation of this principle will require careful consideration of risk/benefit for patient care.
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment' We fully support this principle, and would welcome encouragement through these guidelines for development and widespread availability of rapid point-of-care diagnostics to help prescribers identify bacterial as opposed to viral infection, particularly in primary care settings. Amend existing text to read: 'Promote rapid and/or point-of-care diagnostics for defined patient groups to complement clinical assessment and optimise antimicrobial treatment, including identification of bacterial versus viral infection'
Public/Patients	The role of the public/patients in addressing AMR is critical, and we believe this section could be expanded to identify ways to ensure the public/patients are fully aware of the implications of AMR and their role in prevention – both in taking preventive action to avoid infection (hand-washing, vaccination) and in preventing AMR though proper antimicrobial treatment completion. A shift in mind-set is needed in many countries to encourage patient questioning of need for instead of requesting antibiotic prescription. Insert new text read: 'Complete each antimicrobial treatment course as prescribed 'Practice infection prevention through proper sanitisation and regular vaccination, as recommended by guidelines'
Pharmaceutical industry	'Consider special labelling of antimicrobial packages that identify them as such and indicate that they are medical products for specific use only as prescribed' Placing consideration of special labelling within the remit of the pharmaceutical industry raises the challenge of un-harmonized labelling approaches, creating potential confusion between products with different labels. Standardised language for any special characterization is necessary if a special warning is to be applied, and is typically Health Authority-driven. Differentiated labelling for antimicrobial products should be considered through dialogue with regulatory authorities to ensure a harmonized approach, and possibly is best considered also in the context of a broader public education campaign including patient information materials provided by the pharmacist, online resources, etc.

Section of document	Comment and rationale – proposed change
Norwegian Directorate of Health	
International	'Ensure access to essential antimicrobials by supporting market availability [expert consensus].' Recurrent shortages are a major barrier to access to essential antimicrobials in Europe. Shortages of penicillin G lead to increased use of broad spectrum alternatives. http://www.eahp.eu/sites/default/files/shortages_report05online.pdf https://www.farmanco.knmp.nl/ http://www.legemiddelverket.no/Godkjenning_og_regelverk/Legemiddelmangel_og_avregistreringer/Sider/default.aspx Consider reiterating at healthcare or national and regional level: 'Implement purchasing mechanisms that minimize the risk of shortages of essential antimicrobials'.
Prescribers	'avoid therapy with combinations of antimicrobials unless there is a clear indication according to guidelines [expert consensus]. Example of indicator: proportion of combination treatments among total number of antimicrobial treatments' Proposed indicator could prove perverse in settings where combination therapy is considered to have lower ecological impact than monotherapy, e.g. combination of beta-lactamase-sensitive penicillins and aminoglycosides over carbapenems. Consider removing or limiting proposed indicator.
Norwegian Institute of Public health	
National	'Establish a national committee/platform for the development, implementation and monitoring of clinical guidance for infections [expert consensus].' Regarding the tasks '*the development, implementation and monitoring of clinical guidance for infections*'. It is difficult to understand the tasks for the national committee. This should be clarified e.g. does this only refer to prudent use of antibiotics or does it include development of structures for monitoring of resistance and infection control issues etc. Please clarify
National	'Ensure availability of national clinical guidance based on antimicrobial resistance patterns for the community, long-term care facilities and hospitals' Our interpretation is that this refers to antibiotic use, but please clarify – is there a difference between clinical guidance for infections and clinical guidance. Furthermore, It is important that there are different Guidelines for the different settings. Could this point be merged with point for dentists? Please clarify
Pharmacists	This part should be elaborated. Pharmacists have many roles. In institutions (hospitals and nursing homes) they should take part in the prescribing/clinical team. In many countries pharmacists are not 'qualified to be prescribers' (as defined page 1, line 33), although they have many of the tasks as described in point 5 prescribers, e.g. therapeutic drug monitoring, choice of therapy, reassessment of treatment, changes of formulations/dosing etc. And they advise the prescribers in the therapeutic teams. In the community, pharmacist should be responsible to advise prescribers whenever prescriptions are clearly not in accordance with clinical Guidelines and SPCs. Moreover, to give advice with regard to contraindications and drug interactions, e.g. erythromycin and statins Add new points 1. In hospitals Pharmacists should take part in the prescribing/clinical teams and advise prescribers on appropriate choice, dosing according to Guidelines, co-morbidities, contraindications and drug interactions 2. In the community, pharmacist should be responsible to advise prescribers when the prescription is clearly not in accordance with clinical Guidelines and SPCs Pharmacists should give advice with regard to contraindications and drug interactions, e.g. erythromycin and statins
Nurses	'Be actively involved in antimicrobial management as part of the clinical team by acting as the link with the pharmacy, being responsible for the administration of antimicrobials and for monitoring the patient and patient safety [expert consensus]. Why do we recommend that nurses should be a link with the pharmacy? We should recommend that pharmacists take part in the clinical team.
Pharmaceutical Group of the European Union (PGEU)	
Pharmacists	Suggestions for additional wording to reflect current practice. Pharmacists are the experts in medicines and also are the gatekeepers to the use of antimicrobials. As such, pharmacists can act as an important source of advice and information for patients on the safe, rational and effective use of antimicrobials (including on side-effects, adherence, ADRs, cautions & contraindications, interactions, storage & disposal and rationale for treatment). Pharmacists can be supported with appropriate training, guidelines and information on medicines management, medicines optimisation and provision of pharmacy services (such as services for patients taking new medications, e.g. antimicrobials). Pharmacists can also be supported with access shared electronic health records and/or by being provided with the indications for prescriptions (including antimicrobials) in order to be able to exercise prudence in the prescribing of antimicrobials and managing patient expectations. In several European countries (Ireland, Portugal, the UK and Switzerland) pharmacists administer the seasonal influenza vaccination in pharmacies following appropriate initial and refresher training. As such, pharmacists are able to increase population vaccination coverage and thus reduce inappropriate antibiotic seeking behaviour from those with 'flu symptoms. Add/modify: Current evidence and expert opinion support the following as effective elements of guidelines to support and enable pharmacists in the control and prevention of antimicrobial resistance: a. Do not dispense antimicrobials without prescription, unless specific provisions allow for regulated dispensation in specific circumstances [expert consensus] b. Ensure that the patient understands the dosage and duration of treatment to improve adherence and increase treatment success; promote appropriate disposal of leftover antimicrobials [expert consensus],(medsdisposal.eu) c. Ensure that the patient understands how to benefit most from their treatment, recognise side effects and know what action to take and know what action to take when a suspected ADR occurs d. Participate in local, regional or national public health campaigns concerning the prudent use of antimicrobials. e. Be actively involved in antimicrobial management in the multidisciplinary care team
The Strama Programme Council (Sweden)	

Section of document	Comment and rationale – proposed change
Purpose	There are many very good recommendations in the guidelines but we lack ranking, grading of evidence and cost effectiveness analysis. With our own experience from 20 years of antimicrobial stewardship programs (Strama) in Sweden we would like to highlight the importance of multi professional teams, support from top management and a recognition that this work is not a project but is a part of the core business in modern healthcare
International organisations, agencies	'Establish a new European platform for sharing best practice interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes [expert consensus].' We would like to know more about the ideas behind the proposed European platform
National and regional	'Review, or establish if not available, the legal provisions on availability of antimicrobials over the internet [expert consensus].' Is this really a question for national and regional level? We believe that this must be discussed on the international level within the EU
Healthcare Facilities	The draft report is very focused on hospitals. Prudent use of antimicrobials is very important in hospitals but we think that there should be a special section for community healthcare centres
Prescribers	'take appropriate microbiological samples before initiation of antimicrobial treatment [expert consensus]' We belive that it's important to take appropriate microbiological samples before treatment also in the community
Pharmacists	We would like to add more tasks for the pharmacist 'Responsible for follow up of antimicrobial use' 'Ensure the availability of appropriate antibiotics' 'Ensure good quality in all steps regarding handling of antibiotics'
Nurses	We would like to add more tasks for the nurses 'Remind the clinician that it is time to reassess the antimicrobial treatment after 48-72h in hospitals'
Infection control practitioners	We would like to add more tasks for the Infection control practitioners 'To decrease the incidence of infections requiring antimicrobial treatment, ensure infection control practice guidelines and best infection control practice are implemented in healthcare to prevent healthcare associated infections.'
Public Health Agency of Sweden	
Introduction	It should be mentioned that AMR is a global challenge that needs concerted action, not just a health security issue for Europe. Reference should be given to that this document is aligned (or in accordance) with the WHO Global action plan and the resolution WHA68.7 Rewrite/modify first 2 paragraphs
International organisations, agencies	'Ensure access to essential antimicrobials by supporting market availability [expert consensus].' It is not only about access to essential antimicrobials, it is also about unequal access to useful antimicrobials for common infections with a favourable ecological profile which are not universally accessible within EU, such as isoxazolylpenicillins, mecillinam, nitrofuramtoin etc. Clarify
National	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7].' Controversial if prohibiting the use of certain antibiotics other than to ID specialists or similar has effect on resistance Remove
Healthcare facilities	'A clinician with expertise in the management of infections to be responsible for the antimicrobial stewardship team. A pharmacist responsible for antimicrobial use.' Unnecessary to be so detailed about responsibilities. It may be the pharmacist that could be responsible for the team for example.
Prescribers	'select an antimicrobial with a spectrum of activity as narrow as possible' Modify: 'select an antimicrobial with a spectrum of activity as narrow as possible, in situations when it is considered safe for the patient'
Pharmacists	'Pharmacists are the gatekeepers to the use of antimicrobials and can act as an important source of advice and information for patients, and as such need to be provided with appropriate training, guidelines and information in order to be able to exercise prudence in the prescribing of antimicrobials and manage patient expectations' It is not correct in the Swedish system. Remove or rewrite
Nurses	In countries where nurses manage telephone consultations, their guidance on patient self-care and patient information before a doctor´s appointment can have great impact on the patient´s expectations and doctor´s threshold for prescribing an unnecessary antibiotics. Add
Nurses	Also the logistics in, say, a GP practice can influence final decision on prescribing or not- POC tests should be used appropriately and nurses can play a great role here (strep A only after investigation to confirm, restrictive use of dip-slide in elderly without specific UTI symptoms etc) Add
Pharmaceutical industry	Pharmaceutical industry should not produce/ disseminate treatment guidelines Add
Public Health England (United Kingdom)	
Overall	The comments provided are to enhance the guidelines on prudent use of antimicrobials in human medicine by incorporating the message that prevention of infection is essential as a component of reducing AMR while it is understood the guidelines are not aiming at prevention, it would be valuable to include the prevention messages alongside prudent antimicrobial use messages.
Overall	There is no mention in the whole document of evidence concerning the association between antibiotic diversity/heterogeneity and the selection pressure for resistance. Discuss antibiotic diversity/heterogeneity, especially as this could be a way of prolonging the effectiveness of currently available agents.
Overall	Include a specific section on diagnostics, both point of care testing and laboratory diagnostics, as an important element to improve appropriate prescribing. Suggest that countries develop patient pathways and provide decision support tools to encourage the use of appropriate testing.

Section of document	Comment and rationale – proposed change
Overall - Research	The research topics are very generalised (e.g. 'Promote research on interventional studies for antimicrobial prescribing') and not prioritised. Be more specific and ideally state priorities.
International	'Scientific societies should support the development of good clinical practice guidelines that are adaptable to local resistance patterns and address the most common infections [expert consensus].' Include evidenced based clinical practice guidelines. Scientific societies should support the development of good evidenced based clinical practice guidelines that are adaptable to local resistance patterns and address the most common infections
International and National	There should be reference to European Antibiotic Awareness Day and World Antibiotic Awareness Week. These already exist have been valuable in countries having focused activities and should be included in the document
National and regional	'Establish a national committee/platform for the development, implementation and monitoring of clinical guidance for infections [expert consensus].' It would be valuable to have clarity in this sentence. Clinical guidance for infections should include the treatment/management and also the infection prevention and control of the patient particularly for those with AMR organisms Establish a national committee/platform for the development, implementation and monitoring of clinical guidance for infections that includes diagnostics, treatment/management and infection prevention and control.
National and regional	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8].' Impact of a national campaign on knowledge and behaviour change has been peer reviewed and published and can be included as additional reference Additional reference: Chaintarli et al (2016) Impact of a United Kingdom-wide campaign to tackle antimicrobial resistance on self-reported knowledge and behaviour change http://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-016-3057-2
Healthcare facilities	'Guidelines for the diagnosis and management of infections. Example of indicator: proportion of prescriptions compliant with guidelines.' Guidelines should also include IPC aspects of the infection particularly AMR organisms Guidelines for the diagnosis and management of infections that also includes the infection prevention and control aspects.
Infection control practitioners	1. Amend the title: Infection Prevention and Control (IPC) Practitioners. Terminology incorporates the prevention aspect of the role. IPC and Stewardship should be much more closely linked as they are both integral to prevention of AMR. 2. 'Ensure the collaboration of antimicrobial stewardship programmes and infection prevention and control activities by highlighting the role of appropriate antimicrobial use in the prevention and control of healthcare-associated infections [expert consensus].' This sentence is critical but does not quite outline the collaboration and integration of the two programmes. It gives more weight to stewardship. Suggested wording: 'Ensure the collaboration and alignment of antimicrobial stewardship programmes and infection prevention and control programmes so they are working together at preventing infections and highlighting the essential aspect of appropriate antimicrobial use in the prevention and control of healthcare-associated infections.'
Education/academics	'Ensure that all healthcare professionals are regularly trained on appropriate antimicrobial use [14,46]. Example: require participation in a minimum number of certified education activities on antimicrobial prescribing and use' Essential but misses the opportunity to include infection prevention and control in education and training for healthcare professionals. If infections are prevented in the first place there will be a decreased need for antimicrobials leading to less use and less resistance. Add two points: a. Ensure that all healthcare professionals are regularly trained on infection prevention and control and appropriate antimicrobial use b. Include training on prudent antimicrobial use and infection prevention and control……
Public/patients	'Get informed about appropriate antimicrobial use, antimicrobial resistance and adverse reactions to antimicrobials [expert consensus]' Misses the opportunity to educate the public about the importance of preventing infections. If they play a role in preventing infections in the first place there is less need for antimicrobials. Messages about: -Staying well -Preventing cross infection -Vaccination Get informed about prevention of infection by staying well, preventing cross infection, vaccination and appropriate antimicrobial use, antimicrobial resistance and adverse reactions to antimicrobials
Research	'Promote research that assesses and compares behavioural change interventions for antimicrobial prescribing, taking into account cultural differences, in order to improve our understanding of the optimal ways that rational antimicrobial prescribing practices can be achieved [47]' Misses the opportunity to talk about Infection Prevention and Control and behavioural change interventions Modify: 'Promote research that assesses and compares behavioural change interventions for infection prevention and control and antimicrobial prescribing, taking into account cultural differences, in order to improve our understanding of the optimal ways that rational antimicrobial prescribing practices can be achieved'
Robert Koch Institute (Germany)	
National and regional	'Explore motivational and system change approaches to optimise antimicrobial prescribing.' Rapid and point of care tests are not used if not available/reimbursed. Extension: Explore motivational and system change approaches to optimise antimicrobial prescribing and the use of rapid and point-of-care tests.
National and regional	Access to essential drugs should also be an issue for national governments (e.g. stocks). Add: Ensure access to essential antimicrobials

Section of document	Comment and rationale – proposed change
National and regional	'Establish a national committee/platform for the development, implementation and monitoring of clinical guidance for infections [expert consensus].' What is the rationale behind the introduction of a 'Natl. Committee for clinical guidance on infections' – please explain - shouldn't we rather promote specialist committees focussing on individual infections such as a 'committee on sepsis' writing sepsis guidelines, committee on UTI writing treatment guidelines for ambulatory UTI and so on.
Laboratories	'Ensure that susceptibility testing and reporting are in accordance with treatment guidelines (selective reporting), and European and national standards [expert consensus]. Example: Selective reporting for urinary tract infections [26].' Provision of MICs especially in MDRs Extension:…Example: selective reporting for urinary tract infections (26), *provision of MICs, if therapeutically relevant*
Laboratories	Identification of resistance mechanisms might be of importance for infection control as well as for antimicrobial therapy (e.g. ESBL, carbapenemases). Add: Provide identification of critical resistance mechanisms
Laboratories	Therapeutic drug monitoring plays an increasing role particularly in critically ill patients and in connection with new dosing regiments (e.g. continuous infusion of betalactam-antibiotics) Add: Provision of TDM and timely reporting of results
Laboratories and Prescribers (in the community)	Appropriate sampling is important. We suggest including the following hint: 'Consider to take appropriate microbiological samples at least in those cases in which success of empiric therapy may be uncertain'
Laboratories	We suggest recommending reliable and profound feedback between laboratories and physicians, ID specialists, etc: 'Provide support with respect to correct sampling and interpretation of test results'
Prescribers	'for a patient with sepsis, start antimicrobial treatment via the intravenous route within 1 hour of recognition of sepsis [28]'; 'follow guidance for perioperative antimicrobial prophylaxis [43] and, in particular, administer intravenous perioperative antimicrobial prophylaxis within 60 minutes before incision (except when administering vancomycin and fluoroquinolones), prefer single dose of perioperative antimicrobial prophylaxis, and avoid prolonging antimicrobial prophylaxis after the end of surgery [expert consensus]. Examples of indicators: rate of compliance with administration of perioperative antimicrobial prophylaxis within 60 minutes before incision, rate of compliance with discontinuation' Does not comply with the scope: The report will not cover specific medical conditions…' and is not in line with the systematics of the more general points constituting the rest of this section. Leave out the specific recommendations.
Pharmacists	The contribution of pharmacists might be more comprehensive particularly in hospitals Add: Provision of advice in appropriate administration of antimicrobials (e.g. dosing regimens in critically ill patients, drug interactions)
	The clinical microbiologist might provide essential contributions with respect to the management of infectious diseases (e.g. appropriate prescribing and diagnosis of infectious diseases) Add a section for Clinical microbiologist
	Structures and conditions for routine resistance surveillance activities are not explicitly supported. So far only a few comments highlight this aspect. Please highlight better.
Education/academics	The curricula of certified educations (e.g. medical academic education) should include the respective teaching contents (antimicrobial therapy,..) in a form and scale which is adequate to the importance of antibiotic resistance for the individual patient and public health. National and regional governments, professional associations…are often involved in setting up curricula or learning targets. Therefore, the point 'education' should additionally be included in section 2. In addition, the topic 'education' should be considered in section 2.
Public/patients	Patients in the community not always follow the prescribed administration regimen (stop of therapy directly after cessation of symptoms, lower dose…), which might facilitate development of resistance. Add: Adhere to prescribed drug administration regimen
Research	Please highlight permanent support for addressing research aspects about antimicrobial resistance emergence and spread
Pharmaceutical industry	Recommendations for and points requested from the pharmaceutical industry are only marginal. Could be specified and improved.
Pharmaceutical industry	Increasing occurrence of supply bottlenecks, which might lead to the administration of antimicrobials which are not equally effective, have more side effects, have a broader antimicrobial spectrum than necessary to treat the infection and/or are more expensive. Availability of drugs is already mentioned in section 1, but this is also a responsibility of the pharmaceutical industry. Add: Ensure availability of essential antimicrobial drugs
	Nomination of indicators for an evaluation of the implementation of this guidance document seems incomplete – please improve.
Royal Pharmaceutical Society Antimicrobial Expert Advisory Group	
Pharmacists	Pharmacists are mentioned, as is testing – but there is a real opportunity to do point of care testing for viral/bacterial infections within the community pharmacy. This can help make better use of healthcare resources and help change patient behaviour when it comes to prescribing for self-limiting infections. Add
Pharmacists	Community pharmacists are the last port of call before the prescription gets dispensed in the community, and therefore have an opportunity to reinforce any advice given by the initial prescriber about appropriate use of the antibiotics, advice relating to delayed use, and encouraging patients to take them properly and dispose of the remainder. Add
Pharmacists	There has been some real success with public health campaigns in Canada looking at hypertension where they have provided consistent and frequent messages to all healthcare professionals and patients that has helped to drive down BP rates. The success behind some of their work has been grounded on evidence based practice, consistent messages, and frequency of information. The same should apply to any campaigns around use of antibiotics, of which there is a role for the community pharmacy team Add
Pharmacists	The research elements are very focused on healthcare professionals and molecules themselves. Should some consideration be given to changing patient perceptions as ultimately it is them that drive some of the inappropriate antibiotic prescribing in primary care. Add
Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)	

Section of document	Comment and rationale – proposed change
National and regional	The draft document does not address the recognition of specialists in Infectious Diseases despite international guidelines and documents on antimicrobial stewardship explicitly recognize the relevance of specialists in infectious diseases to improve antimicrobial use in the setting of antimicrobial stewardship programs: 1. USA (Dellit et al. 2007. PMID: 17173212): Core members of a multidisciplinary antimicrobial stewardship team include an infectious diseases physician and a clinical pharmacist with infectious diseases training (A-II) 2. Australia (The role of the infectious disease service. In: Antimicrobial Stewardship in Australian hospitals. 2011): 'Infectious diseases physicians give legitimacy to antimicrobial stewardship programs and play an important role by collaborating with local specialists to ensure that the team's goals are understood and met.' 3. United Kingdom (O'Neill et al. Tackling Drug-Resistant Infections Globally: final report and recommendations. 2016): Key intervention #7. 'Improve the numbers, pay and recognition of people working in infectious disease', explicitely naming infectious diseases doctors.
National and regional	There are still a few (3) countries in Europe (i.e. Spain) in which the Specialty of Infectious Diseases is not recognized by the respective national governments. In addition to the insufficient recognition of people already working in infectious disease, the lack of standardized education in this field leads to insufficient number of specialists who are unevenly distributed along the country, hindering access to expert advice, which is nuclear for antimicrobial stewardship. To include 2 additional elements of national policy /regulatory function: - Ensure recognition of the Specialty of Infectious Diseases and define the education and other requirements needed to achieve this recognition. - Ensure the availability of enough number of specialists in Infectious Diseases in the country/region
	See comments by the Dutch Society for Medical Microbiology (The Netherlands)
Standing Committee of European Doctors (CPME) (Belgium)	
National and regional	'Ensure availability of national clinical guidance based on antimicrobial resistance patterns for the community, long-term care facilities and hospitals [3,4] [expert consensus].' 'Ensure national clinical guidance is reviewed and revised when there is a significant change in antimicrobial resistance, new evidence on management of infections or at regular intervals (e.g. 2–3 years) [expert consensus].' A precondition for doctors to ensure appropriate prescribing of antibiotics is to have access to precise and updated guidelines. The guidelines should provide with a basis for giving the correct antibiotic in the necessary quantity. It should also specify in which infections/cases of illness the patient may/must await natural recovery – and, where necessary, state how many days the patient must wait before consulting the doctor again. Consequently, CPME fully support these recommendations
National and regional	In general, the draft guidelines do not address in detail the issue of point-of-care diagnostics and laboratory tests. However, CPME believes that ensuring access to better and faster diagnostics is a decisive factor to prevent antimicrobial resistance. If the doctor has early confirmation of the patient's diagnosis, it can be avoided that antibiotics are prescribed 'to be on the safe side'. Consequently, national guidelines should also indicate which point-of-care diagnostics and laboratory tests can be carried out in practice in aid of a diagnosis and when a test should be submitted for further bacteriological diagnoses. (new indent) 'Ensure the availability of national guidelines for point-of-care diagnostics and laboratory tests to support the prescriber's decision.'
	In all European countries, only doctors and dentists are allowed to prescribe antibiotics to humans. CPME encourages all countries to enforce these regulations very strictly as the only possible way to control antibiotic consumption. In addition, doctors, dentists and veterinarians should not be allowed to sell antibiotics apart from in pre-existing exceptional circumstances. Consequently, CPME suggest adding a new indent to ensure a strict implementation of national regulation on antibiotic prescribing. (new indent) 'Ensure a strict implementation of national regulations on antibiotics prescribing to humans.'
	'Ensure compliance with the regulations with regards to the dispensing of antimicrobials without prescription and over the internet [expert consensus].' This indent states that national and regional policy shall 'Ensure compliance with the regulations with regards to the dispensing of antimicrobials without prescription and over the internet.' The meaning of this statement is unclear and should be further specified to ensure that a strict framework is in place at national and/or regional level.
Prescribers	Under the prescriber's section, CPME believes that EU guidelines should contain key messages relating to antibiotic prescribing, starting with basic principles before moving on to more specific recommendations. As such, the first indent should emphasise the fact that the prescriber should diagnose the patient in person before prescribing antibiotics, except in exceptional circumstances. (new indent) 'diagnose the patient in person before prescribing antibiotics, except in specific circumstances.'
Prescribers	'for a patient with sepsis, start antimicrobial treatment via the intravenous route within 1 hour of recognition of sepsis [28]' In such circumstances, the draft guidelines provide that an antimicrobial treatment should be started within one hour via the intravenous route. Considering that this statement refers to exceptional cases, CPME would suggest moving it at the end of the sub-section.
Prescribers	'avoid treatment for colonisation without evidence of infection [29] [expert consensus]' For the sake of clarity, we would suggest to specify the sentence as follows : 'avoid treatment for colonisation without evidence of bacterial infection after a relevant clinical and diagnosis examination.'
Prescribers	'inform the patient about their antimicrobial treatment' The prescriber should ensure that patients are well informed that antibiotics must be taken long enough, as their physician has prescribed in order to improve compliance and prevent antimicrobial resistance. Modify: 'inform the patient about their antimicrobial treatment and the importance to respect the treatment duration.'
Public/patients	In line with the previous comment, CPME suggest to also emphasise the importance of compliance under the public section. (new indent) 'respect the treatment duration following physician/dentist's prescription'
Vaccines Europe (Belgium)	

Section of document	Comment and rationale – proposed change
Overall (general comments)	More attention to prevention, including vaccination, should be highlighted in almost every section as one of the tools that can help with the prudent use of antimicrobials to the fight against antimicrobials resistance (e.g., conjugate pneumococcal and influenza vaccines) as highlighted in the UK review paper on AMR 'Vaccines and alternatives approaches: reducing our dependence on antimicrobials' (http://amr-review.org/sites/default/files/Vaccines%20and%20alternatives_v4_LR.pdf) . Notably, by reducing the number of pathogens by vaccination, vaccines can permit the use of narrower-spectrum antibiotics for empirical therapy and resistance is not a significant clinical problem for bacterial infections against which we vaccinate routinely. There is an urgent need for new bacterial vaccines that impact AMR in the human as well as veterinary setting. Both nurses and pharmacists play an important part in vaccinating adults and talking to patients about vaccination. This should be reflected in the text.
Introduction	'Combined with the meagre development of novel antimicrobials, the spread of resistance to existing ones is leading to loss of effective options for the treatment and prevention of infections, representing a health security threat for Europe.' Not just an issue of 'meagre development of antimicrobials' but also poor use of vaccines and need for new vaccines especially in adult populations. Suggested edit '…meagre development of novel antimicrobials and both development of vaccines and implementation of vaccination programmes….'
Introduction	'Antimicrobials are unique among therapeutic medicines…' Poor use of vaccines especially in adult populations. Suggested edit: 'Antimicrobials and vaccines are unique among….'
Definitions	Definition of Antimicrobial stewardship programmes Clostridium difficile is not the only micro-organism taking advantage of anti-microbial treatment to develop. There are other examples, i.e. Candida albicans, E. coli, S. aureus, Klebsiella. It needs to be clarified that AMR is mediated by transmissible genes/gene-products, e.g.: beta-lactamases that are encoded by plasmids that are easily transmissible between bacterial species. This also puts zoonotic bacterial infections in different perspective, i.e. E.coli, S.aureus strains are usually host-specific (humans, pigs, cats, dogs, etc.) but their mobile genetic elements that code for AMR are easily transmissible and can easily pass over various hosts. Add '…in order to limit antimicrobial resistance and to prevent Clostridium difficile or other micro-organisms'
International	Add vaccines, as it is also about ensuring appropriate use of vaccines. In this paragraph the role of international organizations and agencies is described as controlling and preventing cross-border spread of anti-microbial resistance. Therefore promotion of prevention should be part of the list of activities, including vaccination because limiting infections/diseases mechanically limits the need for anti-microbials, so the resistance as well. Vaccination not only provides direct protection to individuals against a disease, but also, for some diseases, inhibits carriage (the colonisation of an individual in the absence of disease) or limits spreading of infections within a community (herd immunity). Linked to easy global transmission of bacteria but also the transmission of mobile genetic elements coding for AMR between hosts, multinational efforts for stewardship with respect to the use of antibiotics in clinical settings/pharmacies in low and middle income countries is a challenge and needs at least to be put on the agenda as a challenge. Suggested edit: Each of the letter bullets should support not just antimicrobial, but also vaccine use. E.g. '…. to support appropriate antimicrobial and vaccine use.' To add a new point: 'Promote prevention, including vaccination programs with a life-course approach'
National and regional	'Integrate national antimicrobial stewardship activities into the national antimicrobial resistance plans that include infection prevention and control and vaccination, in a 'One Health' approach [expert consensus].' Need clarification of b. and link to national immunization plans as nationwide use and widespread promotion of high immunization coverage by public health authorities can affect anti-microbial resistance. Add a new bullet saying: 'Improve vaccination coverage in all age groups, through a life-course approach, in order to reduce the use and misuse of antibiotics and in alignment with national plans for the fight against AMR. National AMR plans should include the necessity to evaluate and review national immunization plans, potentially expanding age-range for existing vaccines or including new vaccines with the potential of limiting the use of anti-microbials'.
National and regional	'Set qualitative and quantitative targets for improvement of prescribing [expert consensus]. Example: antibiotic quality premium (NHS England) [2].' Setting qualitative and quantitative use for antibiotics should also be supported by improvement of practice and performance in vaccination uptake and coverage rates, which have been demonstrated to reduce AB use. 'Set qualitative and quantitative targets for improvement of prescribing and vaccine coverage rates'.
National and regional	'Ensure availability of national clinical guidance based on antimicrobial resistance patterns for the community, long-term care facilities and hospitals [3,4] [expert consensus].' National clinical guidelines should include recommendation of vaccination to reduce AB use 'Ensure availability of national clinical guidance based on antimicrobial resistance patterns and vaccine coverage for community, long-term care facilities and hospitals'
National and regional	'Fund, design, implement and assess national campaigns on antimicrobial use targeting the public and health professionals [8]' National campaigns for antibiotic use should also be supported by national campaigns for increased vaccination uptake. Publicly linking increased vaccination with reduce AB use and therefore reduced AMR would send a strong message to the public. 'Fund, design, implement and assess national campaigns on antimicrobial and vaccines use targeting the public and health professionals'.
National and regional	'Explore incentive systems for appropriate prescribing [expert consensus] [9]' To take a systems approach to reduce AMR it would be wise to explore both incentive systems for appropriate prescribing and increased use to vaccines. 'Explore incentive systems for appropriate prescribing and increased vaccine coverage rates'.
National and regional	'Monitor and audit the appropriate use of antimicrobials introducing relevant quality indicators and set up systems for monitoring these indicators. Ensure regular feedback of the results to prescribers [expert consensus].' It would be important to build evidence of vaccination approaches, which have led to a successful impact on AMR, allowing for best practice exchange. 'Monitor and audit the appropriate use of antimicrobials introducing relevant quality indicators, including the effects of vaccination on AMR, and set up systems for monitoring these indicators. Ensure regular feedback of the results to prescribers'.
National and regional	'Explore motivational and system change approaches to optimise antimicrobial prescribing.' Motivation is needed also to increase vaccination rates. 'Explore motivational and system change approaches to optimise antimicrobial prescribing and increase vaccine recommendation by HCPs and coverage rates'.
National and regional	Important to strengthen vaccination programmes, given the value they have to decrease unnecessary use of antibiotics. Suggest new bullet that speaks to the need to improve vaccination programs: 'Strengthen vaccination programmes to support improved access to vaccines for all age groups as a means to decrease unnecessary use of antibiotics.'

Section of document	Comment and rationale – proposed change
Healthcare facilities	'Guidelines for the diagnosis and management of infections' Modify: 'Guidelines for the diagnosis, prevention and management of infections'
Healthcare facilities	'Documentation in the patient chart of indication, drug choice, dose, route and duration of treatment [expert consensus].' Documentation in the patient chart of indication, drug choice, dose, route and duration of treatment Patient chart should also include comorbidities and vaccination history Add: '…. comorbidities and vaccination history'
Healthcare facilities	'Monitoring of quality indicators and quantity metrics of antimicrobial use with feedback to prescribers and prescriber actions agreed' Monitoring of quality indicators and quantity metrics of antimicrobial use Quality indicators should include measurement of prevention activities such as hand-washing compliance, use of masks, vaccination etc. Add new point: 'Monitoring of prevention activities and compliance with the National Immunization Programs (especially regarding recommendations for HCPs)'
Healthcare facilities	'Establish a multi-faceted approach that may include elements such as clinic-based education, patient information leaflets [25] and public patient education campaigns combined with clinician training [21] in communication skills.' A multi-faceted approach should include prevention of infections in both patients, and health-care professionals, for both their own protection and the risk of transmission to patients through health-care professionals. Add education campaigns re: 'prevention of infections, including through vaccination, directed towards hospital staff and patients'.
Prescribers	Prescribers should also support and encourage vaccination use against pathogens to help prevent unnecessary use of antibiotics. Suggest new sub-bullet 'Support increased use of vaccination to minimise the unnecessary use of antimicrobials.'
Prescribers	'consider relevant host factors: age, immune status, renal function, allergies, foreign bodies and risk factors for antimicrobial resistance (e.g. history of recent antimicrobial use, history of recent travel) [expert consensus]' Vaccination status could also be a risk/protective factor that could be documented. Knowing immunization status can permit the use of narrower-spectrum antibiotics for empirical therapy. The words 'immune status' should be clarified. Does this mean risk (i.e. immune competence) or vaccination status? 'Consider relevant host factors: age, vaccination status, immune status etc. '…(e.g. history of recent antimicrobial resistance , immunization history….' The words 'immune status' should be clarified.
	'consider delayed antimicrobial prescribing with appropriate safety netting for adults or children in specific circumstances and according to guidelines [36-38].' Take into account the vaccination status of the patient (vaccinated children) for delaying AM treatment. Suggest edit: 'According also to the patient's vaccination status, consider delaying (…)
	Prescribers should follow their national infection control policies in reducing dissemination of infections including prevention by vaccination. Suggest new bullet in the community section: 'Prescribers should follow their national infection control policies in reducing dissemination of infections including prevention by vaccination.'
	In the community, prescribers also have a role in following National Immunization Plans Add. 'Ensure all patients are offered and whenever feasible receive the recommended vaccines according to the National Immunization Plans'.
Pharmacists	In some EU countries pharmacists are playing an important role in education, promotion of prevention, and vaccination programs. Add 'Promote infection prevention'.
Nurses	The role of nurses should be expanded to provide vaccines as a means to increase uptake and avoid unnecessary infections. Suggest new sub-bullet 'Support policies that enable nurses and other trained healthcare professionals to serve as vaccinators as a means to increase vaccination access and decrease AMR.'
Infection control practitioners	What does 'infection prevention' mean? Clarify ' infection prevention'
Education/academics	'Require participation in a minimum number of certified education activities on antimicrobial prescribing and use' Important that all providers also understand the appropriate use of vaccines and the role they play in minimising unnecessary use of antibiotics. Suggested edit: '…require participation in a minimum number of certified education activities on infection prevention and control, and more specifically on antimicrobial prescribing and use and vaccine use.'
Public/patients	'Get informed about appropriate antimicrobial use, antimicrobial resistance and adverse reactions to antimicrobials [expert consensus]' Important that patients also understand the appropriate use of vaccines and the role they play in minimising unnecessary use of antibiotics. Suggested edit: 'Get informed about appropriate antimicrobial use, antimicrobial resistance, ~~and~~ adverse reactions to antimicrobials, and value of vaccines to preventing unnecessary use of antibiotics.'
Research	The importance of research for new vaccines targeting bacterial infections is missing Add the following bullet point: 'Promote research in preventive measures and tools that will reduce our dependence on antibiotics, including improved infection control and vaccines against community and hospital acquired infections and viral or parasitic infections.'
Research	All countries should participate in the clinical development of new vaccines with a role in AMR prevention, and document the impact of the use of vaccines on anti-microbial use and AMR. Insight in the transmission of AMR bacteria and their transmissible genetic elements needs to be expanded, including the veterinary sector. Modeling the impact of vaccines used in health-care settings (nosocomial vaccines), in the general population, taking impact on transmission into account, the use of vaccines in the veterinary sector etc. The development of novel regulatory paths towards licensure of vaccines with an impact on AMR need to be explored, including the establishment of immunological correlates of protection that can be used as licensure criteria Add. 'Participate in the clinical development of new vaccines with a role in AMR prevention, and document the impact of the use of vaccines on anti-microbial use and AMR'.
Research	Cost-effective strategies could help prioritize interventions Add: 'Promote cost-effectiveness analysis'

Comments from individuals

Section of document	Comment and rationale – proposed change
Paediatrician (Spain)	
International	Implementar indicadores más adecuados para medir el consumo en población infantil. Los indicadores actuales, sobre todo el DDD, no reflejan adecuadamente este consumo porque, entre otros, el número de envases de presentaciones orales tiende a sobrevalorar el consumo Conocer el consumo real de antibióticos en población infantil
National and regional	Asegurar para los prescriptores unas condiciones de trabajo que permitan dedicar a cada paciente el tiempo suficiente para realizar un correcto diagnóstico, utilizar en su caso, pruebas diagnósticas precisas, explicar al paciente la actitud a seguir, la evolución esperable y, en su caso, el motivo por el que se prescribe o no se prescribe Disminuir la incertidumbre terapeútica en el prescriptor Aumentar la educación de los pacientes e incentivar el autocuidado
National and regional	Poner a disposición de los prescriptores una guia de antibióticos actualizada, revisada periódicamente que incluya mecanismo de acción, resistencias microbianas e indicaciones aprobadas, aceptadas y recomendadas incluyendo pediatría y mencionando otras alternativas si las hubiere Mejorar la información y, por tanto, la formación, de los prescriptores
National and regional	Poner a disposición de los prescriptores información disponible y de utilidad clínica sobre resistencias clínicamente relevantes en los gérmenes más frecuentes en el ámbito local, estratificada según edades, origen de muestras (atención primaria u hospital)
National and regional	Actitud coordinada de todas las instituciones, organismos y sociedades científicas implicadas Emisión del mismo mensaje por parte de todos para reforzar su impacto a todos los niveles
National and regional	Dotar a cada prescriptor de los medios legales y administrativos precisos para realizar la prescripción Disminuir la prescripción inducida Responsabilizar a cada prescriptor de su prescripción
Healthcare facilities	dotar a los prescriptores, no solo en hospital, también en atención primaria de pruebas de diagnóstico rápido y de acceso a pruebas de diagnóstico microbiológico y a sus resultados en el más breve plazo posible Disminuir la incertidumbre diagnóstica Prescripción de tratamientos ajustados a la patología diagnosticada
Nurses	Considerar que la formación actual de las enfermeras no es igual en todos los países de la EU y por tanto en algunos casos no será suficiente para poder considerarlas como prescriptoras de estos fármacos Mejorar la formación de los prescriptores
Research	Estimular y favorecer la investigación sobre uso, consumo, utilización de pruebas diagnósticas, prescripción y mejora de la prescripción en atención primaria, ámbito en el que se realiza un mayor número de prescripciones y en el que la sobrecarga de trabajo y , a veces la dispersión de los profesionales dificulta el desarrollo de proyectos de investigación Además la investigación en atención primaria se debe dirigir a procesos, intervenciones y actividades distintos de los atendidos en centros hospitalarios por lo que es necesario conocer los datos reales en este medio sin el sesgo que existe en los estudios realizados en medio hospitalario Destinar recursos, formación y fondos específicamente a este apartado
Research	Estimular y favorecer la investigación sobre uso, consumo, utilización de pruebas diagnósticas, prescripción y mejora de la prescripción específicamente en pediatría, en población pediátrica y específicamente también en atención primaria. Los pediatras son menos numerosos que los médicos que atienden a adultos y la sobrecarga de trabajo, la dispersión y el aislamiento es aún mayor en estos profesionales y mayor que el de los pediatras que trabajan en hospitales Además la investigación en población infantil en atención primaria se debe dirigir a procesos, intervenciones y actividades realizadas en este medio, sin el sesgo que existe en los estudios realizados en medio hospitalario Destinar recursos, formación y fondos específicamente a este apartado
Clinical pharmacist (Hungary)	
Acknowledgments	Lack of several stakeholders (i.e. pharmacists, nurses) provide graduation background for each expert
Definitions	'Antimicrobial stewardship programmes': not only C.difficile but also MRSA and others delete C. diff or add few more examples
Principles and elements...	'Ensure access to essential antimicrobials by supporting market availability' Not only essential antimicrobials are needed. In some countries narrow spectra agents are not available any more.....this is a mistake from the national health authority which can be reversed if it there is a rule at a higher (EU) level to 'remarket' it. add: access to narrow spectra agents
	Add: advertisement of antibacterial soaps/local OTC antibacterials should be limited
National and regional...	'Establish a national committee/platform for the development, implementation and monitoring of clinical guidance for infections [expert consensus].' Funding is also critical element. Add: Establish and fund national committee
	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7].' First international (e.g. essential antibacterials) list is needed then it should be adopted to national needs/resistance patterns. Should be also in accordance with the WHO critically important antimicrobials list Rephrase the sentence
Healthcare facilities	'An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv).' Please provide the minimum number of healthcare professionals with this role per 100 bed add number to text

Section of document	Comment and rationale – proposed change
Prescriber	many of these activities is also the role of simple community pharmacist without prescribing authority (e.g. role ii; xi;xii) or hospital pharmacist's! (e.g. from role iv. to role x) See also the document of the FIP which focus on community pharmacists: AVAILABLE AT: https://www.fip.org/files/fip/publications/2015-11-Fighting-antimicrobial-resistance.pdf add to pharmacists's section these roles prevention: education of hygienic rules (sneezing etiquette), vaccination of adults (e.g. influenza Portugal, Ireland, Belgium, etc) triage function, symptomatic treatment in hospitals even more role: find, optimise, adjust treatment (dosage, spectra, administration route, drug allergy), TDM interpretation, develop protocols, provide utilisation data...see a good stewardship program
Pharmacist	controversial thing: you say that pharmacists are one of the key persons in the AMR team and here you only give this two (questionable...see notes below) roles...they have many other roles. See also previous note add roles listed in the FIP document and also roles that are commonly practised by hospital pharmacists
	'Ensure that the patient understands the dosage and duration of treatment and promote returning leftover antimicrobials to the pharmacy The message of this sentence is quite doubtful….The literature says that around 20-50% of prescriptions in primary care are superfluous and also many times therapy duration is not indicated at all on the prescription....so why should pharmacist emphasize to adhere to this superfluous/or not defined length AB therapy...This whole action on pharmacist advice 'take antibiotics after you feel well' had also a negative effect...pharmacist also parroting these rules when only 1 dose is needed (e.g. prophylaxis for dental procedures) and when in reality AB would not be needed et al…. Consider rephrasing
Nurses	Also other roles: ensure adherence to therapy, avoid side effects (e.g. slow administration of vancomycin to prevent red-man syndrome)
Education	independent education/educator is needed add to text Specify the minimum number of hours and topics to be covered in each curriculum add to text
Appendix 2	Be more specific. For most of these indicators, target values could be easily set up. Without it, it is not ready for use Consider adding target values.
Hospital pharmacists (France)	
International	Need to add infection prevention and control and promotion of vaccination
National and regional	'Establish a list of antimicrobials with restrictive measures for use [expert consensus] [4,6,7]. ' A statement could be added for shortages on antimicrobial by the National medicine Agency and which replacing antimicrobial could be used instead Add: Ensure availability of needed antimicrobial agents; Establish a program to prevent and address antimicrobial shortages (preparedness and response: dissemination of list of replacement medicines or of temporary prescribing guidance).
National and regional	'Ensure availability of standardised local and national open data for benchmarking [expert consensus].' Surveillance system of microbiological and resistance patterns at a country level ADD: Establish a surveillance system to monitor microbiological and resistance patterns at a national level in community and hospital sector. Surveillance system of antimicrobial use at a national level in community and hospital sector Add: Establish a surveillance system to monitor antimicrobial use and consumption at a national level in community and hospital sector.
Healthcare facilities	Antimicrobial stewardship programmes should be linked with the infection prevention and control programme and/or the patient safety programme
Healthcare facilities	Definition of IT and details on what it could include Antimicrobial stewardship activities, including electronic prescription and tools to allow for pharmaceutical analysis, dispensation.
Healthcare facilities	Vaccination promotion for preventable diseases Promote effective vaccination for preventable diseases.
Prescribers	Antibiotic treatment is avoided for viral infection but not antimicrobials (considering the definition of antimicrobial Page 1)
Prescribers	'select an antimicrobial in accordance with available guidelines, at an appropriate dose and for the shortest effective duration' The route of administration is part of optimal use of antimicrobials … an appropriate dose, for the shortest effective duration and with appropriate route of administration (preferably with oral route when possible)
Prescribers	Comorbidities could be relevant host factors Please include in host factors
Prescribers	Think about alternative option other than antimicrobial therapy Consider alternative prescribing options when there is a bacterial infection e.g. fecal microbiota transplantation

Section of document	Comment and rationale – proposed change
Pharmacists	Difference between pharmacists in community and in hospitals needs to be underlined as for prescribers. In hospitals, the role of pharmacists in Antimicrobial stewardship is essential, as highlighted recently by the Gallagher team (Heil EL, Kuti JL, Bearden DT and Gallagher JC. The essential role of pharmacists in Antimicrobial Stewardship. Infection Control & Hospital Epidemiology/Volume 37/Issue 07/July 2016, pp 753 – 754). Another reference could be added: International Pharmaceutical Federation (FIP). Fighting Antimicrobial Resistance: The Contribution of Pharmacists. 2015 http://fip.org/files/fip/publications/2015-11-Fighting-antimicrobial-resistance.pdf Modify as follows: In the community : - Do not dispense antimicrobials without ~~a~~ prescription , unless specific provisions allow for regulated dispensation in specific circumstances (expert consensus) - Promote and participate to patient education program on optimal use of antimicrobial agents, antimicrobial resistance, vaccination and hygiene; perform rapid-diagnostic test and vaccination according to local regulations - If needed, address patients to a GP or hospital for a specific consultation - Ensure that the patient understands the dosage and duration of treatment and promote returning leftover antimicrobials to the pharmacy - Assess the prescription according to the medical file (if provided) - Notify adverse-events related to antimicrobials according to regulation In hospitals : - Do not dispense antimicrobials without prescription, unless specific provisions allow for regulated dispensation in specific circumstances (expert consensus) - Assess the prescription according to the indication and local organization for antimicrobial use (e.g. pre-authorisation for some antibiotics, restricted dispentation…) - Assess the prescription after 48-72h according to microbiological and resistance patterns, and alert the Infectious Diseases specialist for targeted antibiotics or if necessary - participation to the Antimicrobial Stewardship Team for the pharmacist responsible for antimicrobial use (audits, monitoring of quality indicators and quantity metrics of antimicrobial use (defined daily doses DDD for example) with feedback to prescribers and definition of actions for improvement, updating protocols, prescribers training) - Update a list on antimicrobials shortages and propose alternatives if necessary - Notify adverse-events related to antimicrobials according to regulation - Promote and participate to healthcare workers and patient education program on optimal use of antimicrobial, antimicrobial resistance, vaccination and hygiene
Public/patients	Public should also be informed on infection prevention and control, the benefit of vaccination and the normal course of common viral infections Add: Get informed on how to prevent infections and reduce the need for antimicrobial treatments (hygiene, vaccination) and on the normal course of common viral infections.
Public/patients	'Do not use antimicrobials without a medical prescription' Add: and avoid self-medication
Public/patients	'Do not use leftover antimicrobials' Patients have to return left-over to the community pharmacy in order not to self-medicate. Add: and return them to the pharmacy
Research	To tackle AMR, one way is to promote research on innovation on a new class of antibiotics or new molecules or therapeutic class to treat bacterial infections Add: Promote innovation on new drugs to tackle AMR
Pharmaceutical industry	Pharmaceutical industry has the role of finding new drugs and promotes them. Consequently this aspect has to be considered in a delinkage initiative to orientate research and development to priority health needs with rewards on innovation Add: Promote delinkage initiative to orientate research and development to priority health needs with rewards on innovation
Respiratory Medicine and Intensive Care consultant (Portugal)	
Definitions	The objective of stewardship programmes is to prevent all hospital-related infections (e.g. *C. difficile*, MRSA, carbapenemases, etc.) and NOT only *C. difficile* infections
Education/Academics and Public	more focus on hand washing and infection control measures, prevention and vaccines Ensure that all healthcare professionals are regularly trained on hand washing and infection control measures Ensure that all healthcare professionals are regularly trained on prevention of infections and the importance of vaccination (e.g., flu) Get informed about the impact of hand washing, infection control measures (e.g., respiratory precautions when coughing and sneezing) and vaccines.
Infectious diseases specialist (Spain)	
Definitions	In Spain midwives and nurses are not considered prescribers by law Add: Local and national regulations
Definitions	Dental practitioners belong mostly to the private medical practice in Spain and are a matter of concern related to antimicrobial prescription out of the public health system. Qualified dental practitioners is to suppose too much. But in line 87 page 2 could be a solution (practice guidelines for dentist).
International	'Establish a new European platform for sharing best practice interventions on appropriate antimicrobial use and their impact on relevant qualitative and quantitative outcomes' Sharing best practices or sharing best evidence supported or based practices? Clarify Please define quantitative outcomes
International	'Encourage the development of European and national standards for selective reporting of microbiology results to optimise antimicrobial prescribing [expert consensus].' Selective reporting means filters to the antibiotic susceptibility results? Clarify
International	'Develop European evidence-based guidelines on the use of rapid and point-of-care diagnostics [expert consensus].' Rapid and point of care diagnostics have no good gold standards for grading evidence needed to develop an evidence-based guideline. Are contradictory terms talking about guidelines and perhaps should be avoided.

Section of document	Comment and rationale – proposed change
National and regional	'Explore incentive systems for appropriate prescribing' Targets for improvement Incentives for healthcare professionals (in an economic crisis sounds difficult) - save money - spend less money - reduce budget of antibiotics How do these results revert to the healthcare pocket? A premium should be controversial Define appropriate prescribing, term too wide too ambiguous
National and regional	'Ensure availability of national clinical guidance based on antimicrobial resistance patterns for the community, long-term care facilities and hospitals' In some countries data from long term care facilities are scarce. Most of them are private centres without an appropriate medical coverage. Knowledge and results about resistance patterns in long-term care facilities should be improved and mandatory reported by all kinds of institution public or private.
National and regional	'Review, or establish if not available, the legal provisions on availability of antimicrobials over the internet' Legal provisions on availability of antimicrobials over the internet Illegal in my country and controversial at least in conflict of interest with the industry.
National and regional	'Consider behavioural interventions to reduce inappropriate antimicrobial prescribing. Such interventions include, for example, accountable justification and peer comparison' Accountable justification and peer comparison Prescription audit performed by the PROA´s team in each hospital?
National and regional	'Explore motivational and system change approaches to optimise antimicrobial prescribing. Example: reimbursement policies to discourage inappropriate prescribing and unnecessary doctor consultations for minor infections and public commitment' Add: …, unnecessary doctor consultations……and unnecessary request of diagnostic tests (microbiological, serological and expensive molecular tests)
Healthcare facilities	Define the term 'clinician' Specify clinical microbiologist, infectious disease specialist or internist
Healthcare facilities	'IT support for antimicrobial stewardship activities' What kind of support is IT support? The budget for antimicrobial stewardship activities will be withdrawn from …?
	There is no word, no mention to the isolation and control measures nor the follow-up cultures to avoid the spreading of resistant microorganisms.
Laboratories	'Ensure that susceptibility testing and reporting are in accordance with treatment guidelines (selective reporting), and European and national standards [expert consensus]. Example: Selective reporting for urinary tract infections' According to EUCAST (or CLSI?)
Prescribers	'therapeutic drug monitoring is recommended for adjustment of the dosing regimen according to guidelines and in specific circumstances.' Should be done in the lab or in the hospital pharmacy? It poses another expensive task to invest
Pharmacists	'Ensure that the patient understands the dosage and duration of treatment and promote returning leftover antimicrobials to the pharmacy' In Spain nobody takes back outpatient medications. Add: Promote mono-dose system and e-prescription, and electronic receipt.
Nurses	'Be actively involved in antimicrobial management as part of the clinical team by acting as the link with the pharmacy, being responsible for the administration of antimicrobials and for monitoring the patient and patient safety [expert consensus].' Add: Promote different to antimicrobials strategies for caring chronic wound and ulcers, and the properly use of antiseptics.
Infection control practitioners Education/academics	Promoting and teaching activities about isolation and prevention measures with multidrug-resistant colonized patients.
Hospital pharmacist (Spain)	
Prescribers	'therapeutic drug monitoring is recommended for adjustment of the dosing regimen according to guidelines and in specific circumstances. Example: therapeutic drug monitoring for aminoglycosides and vancomycin' Rationale: Strong evidence is available about the benefit of therapeutic drug monitoring of some azole antifungals. Therapeutic drug monitoring of azoles should be considered (Ashbee HR, Barnes RA, Johnson EM, Richardson MD, Gorton R, Hope WW. Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology. J Antimicrob Chemother 2014; 69: 1162-76). (Strong evidence for voriconazole, itraconazole and posaconazole).
Research	Special populations are generally excluded from clinical trials of antimicrobials. Additionally, the information about the behavior of older antimicrobials is limited in these populations. Add: Promote research studies of antimicrobial therapeutic drug monitoring in special populations (example: critically ill patients, burned patients, paediatric patients, patients ongoing continuous renal replacement therapy, etc.)
Clinical microbiologist (Bulgaria)	
Introduction	'Combined with the meagre development of novel antimicrobials, the spread of resistance to existing ones is leading to loss of effective options for the treatment and prevention of infections, representing a global health security threat for Europe.' (This is not limited to Europe!). Security threat for Europe and the whole world.

Section of document	Comment and rationale – proposed change
Introduction	'Antimicrobials are unique among therapeutic medicines because their use affects not only the person receiving the treatment but also the rest of the population, including other patients, through a complex effect on microbiota in the human host, other animal hosts and the environment' Not only other patients, but all people, e.g. their relatives, colleagues etc; 'other animals hosts', different from humans'!? The complex effect on microbiota is not as important as the epidemic spread of resistance. The idea that antibiotics are 'societal drugs' belongs to Prof. Stuart Levy and he should be cited here! Modify: population, including other people, and even the future generations [1], through epidemic disseminations of resistant genes and bacteria among humans, animals and environment. [1] Levy BS. The Antibiotic Paradox: How the Misuse of Antibiotics Destroys Their Curative Powers. 2nd Edition, 304 p, Cambridge, Mass, Perseus Publ, 2002
Definitions	Definition of antimicrobial resistance as the resistance of a microorganism to an antimicrobial agent that was originally effective for treatment of infections caused by this microorganism. (this is not true and not scientific)
Definitions	'Prudent or appropriate antimicrobial use aims to benefit the patient while at the same time minimises the probability of adverse effects and promotion of the emergence or spread of antimicrobial resistance.' more clear, how 'to benefit'! Modify as: aims to optimally cure the patient…
Definitions	'Antimicrobial stewardship programmes refer to coordinated programmes that implement interventions to ensure appropriate antimicrobial prescribing and effective antimicrobial treatment, in order to limit antimicrobial resistance and to prevent Clostridium difficile infections.' (There are 2 main aims – improved therapy and limited side effects, incl. to prevent development of resistance and Cl. difficile, however 'the effective treatment is to cure infection, not 'in order to limit resistance') Modify: ensure appropriate antimicrobial prescribing to guarantee effective antibiotic treatment/ prophylaxis, while to contain antibiotic resistance and prevent the side effects, incl. Clostridium dificile infections
Purpose Scope	You refer to the document as 'draft technical report', 'report'. Change with the term 'Guidelines'
Healthcare facilities	An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv)' In USA and in some EU countries pharmacists are leaders in antibiotic stewardship and surveillance of antibiotic consumption, but in other countries (e.g. Bulgaria) these are microbiologists; moreover microbiologists are the most competent in Antimicrobial resistance) Replace pharmacist with microbiologist
Laboratories	Laboratories play a role… (exactly clinical microbiology laboratories, not the other). Modify as: Clinical Microbiology laboratories play…
Pharmacists	Pharmacists are the gatekeepers to the use … I am afraid that a small minority of pharmacists are the gatekeepers… Modify as: Pharmacists are an important link in the chain of the use…
References	I do not consider this is the best collection of publications. I already suggested to be included the SB Levy's Antibiotic paradox. I know other researchers who contributed to the rational antibiotic policies development and I can not see their articles, e.g. Ian M. Gold, who worked as a pioneer in this issue, and was a chair of ESGAP.) Add reference: Levy BS. The Antibiotic Paradox: How the Misuse of Antibiotics Destroys Their Curative Powers. 2nd Edition, 304 p, Cambridge, Mass, Perseus Publ, 2002
General practitioner (Spain)	
Healthcare facilities	'Promote rapid and/or point-of-care diagnostics for defined patient groups' However, availability of these POCT considerably varies across countries and policymakers should provide these POCT in the consultations. Add a new bullet point at National level recommending governments or policymakers the provision of evidence-based high-quality point-of-care tests in the healthcare facilities.
Healthcare facilities	'The availability of facility-specific cumulative susceptibility reports for common bacterial pathogens against antibiotics that are recommended in the guidelines' The availability of facility-specific cumulative susceptibility reports for common bacterial pathogens against antibiotics, is now only available for hospitals in the doc but not for primary care and I find this information crucial for better prescribing antibiotics in primary care. Add a new bullet point also for primary care encouraging the availability of periodic 'local' susceptibility reports for common bacterial pathogens in the community against common antibiotics and provide GPs with this information.
Prescribers	'If antimicrobial treatment is not considered necessary, give patients advice about the expected natural history of the illness, the limited or absent benefit of antimicrobial treatment, and the potential unwanted side-effects of antimicrobials such as diarrhoea and rash, as well as advice about actions in case of worsening clinical condition (safety netting)' I find this information vague or incomplete as prescribers should explain these severe 'signs and symptoms' to patients. Include clear information about when patients should be concerned about this infectious disease; i.e. signs and symptoms of severity and when they should seek medical advice.
Prescribers	Consider pregnancy status as another of the 'relevant host factors'. Include it in this point bullet.
Prescribers	'Reassess antimicrobial treatment and consider modification (e.g. de-escalation, discontinuation or switch to oral treatment) after 48–72 hours in hospitals, and in specific circumstances in other settings according to guidelines'. I miss a crucial point in primary care, mainly for southern and eastern countries, in terms of discontinuing dubious ongoing antimicrobial regimens which had previously been prescribed by another health professional (emergency departments, dentists, private sector, etc) or had been taken by the patients themselves. Include a specific point bullet like this: Encourage the discontinuation of an ongoing antimicrobial therapy for patients, either 1. diagnosed of clinical conditions for which antibiotics are not necessary, 2. or diagnosed of clinical conditions for which antibiotics might be necessary but according to the history and clinical examination the GP considers that antibiotics are not needed to be taken or the patient feels that the antibiotic regimen has not worked as expected and feel they need a clinical reassessment, 3. or have taken some doses of an antibiotic (from leftovers found at the household or obtained at the pharmacy without any medical prescription) for a clinical condition for which antibiotics are not necessary.

Section of document	Comment and rationale – proposed change
Prescribers	There is now a point only for pharmacists encouraging them to ensure that the patient understands the dosage and duration of treatment and promote returning leftover antimicrobials to the pharmacy. This information should also be given in the consultation, since drug-adherence is very low and this permits the existence of leftovers. Add a similar bullet point for prescribers encouraging GPs provide this information to patients. A clear information about the risks of storing antibiotics in the households should be included.
Preventive medicine specialist (Spain)	
Healthcare facilities	Among the indicators it can be included other derivatives of Point-Prevalence Survey of Healthcare–Associated Infections such as EPINE EPPS : percentage of patients with infection associated with healthcare, percentage of patients admitted in hospital with antimicrobial agents, percentage of patients admitted with carbapenem, percentage of patients admitted with linezolid
Infectious diseases specialist (Spain)	
National and regional	The draft document does not address the recognition of specialists in Infectious Diseases despite international guidelines and documents on antimicrobial stewardship explicitly recognize the relevance of specialists in infectious diseases to improve antimicrobial use in the setting of antimicrobial stewardship programs: 4. USA (Dellit et al. 2007. PMID: 17173212): Core members of a multidisciplinary antimicrobial stewardship team include an infectious diseases physician and a clinical pharmacist with infectious diseases training (A-II) 5. Australia (The role of the infectious disease service. In: Antimicrobial Stewardship in Australian hospitals. 2011): 'Infectious diseases physicians give legitimacy to antimicrobial stewardship programs and play an important role by collaborating with local specialists to ensure that the team's goals are understood and met.' 6. United Kingdom (O'Neill et al. Tackling Drug-Resistant Infections Globally: final report and recommendations. 2016): Key intervention #7. 'Improve the numbers, pay and recognition of people working in infectious disease', explicitely naming infectious diseases doctors.
National and regional	There are still a few (3) countries in Europe (i.e. Spain) in which the Specialty of Infectious Diseases is not recognized by the respective national governments. In addition to the insufficient recognition of people already working in infectious disease, the lack of standardized education in this field leads to insufficient number of specialists who are unevenly distributed along the country, hindering access to expert advice, which is nuclear for antimicrobial stewardship. To include 2 additional elements of national policy /regulatory function: - Ensure recognition of the Specialty of Infectious Diseases and define the education and other requirements needed to achieve this recognition. - Ensure the availability of enough number of specialists in Infectious Diseases in the country/region
Infectious diseases/infection control specialist (Austria)	
	This is an excellent and ambitious piece of work. The content is very practical. Highlighting of strategic recommendations for national and regional leaders may be useful. Thank you for making the effort and the manuscript.
Introduction	'Antimicrobials are unique among therapeutic medicines because their use affects not only the person receiving the treatment but also the rest of the population, including other patients, through a complex effect on microbiota in the human host, other animal hosts and the environment' There are many reasons for the prudent use of AB besides this one, e.g. possible harm to the patient because of futile treatment, microbial resistance evolution etc. Omit this phrase.
Definitions	The ASP effect on AMR is controversial and only one reason for ASP. The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as Clostridium difficile), and the emergence of resistance. (Dellit CID 2007)
National	'Ensure availability of national clinical guidance based on antimicrobial resistance patterns for the community, long-term care facilities and hospitals [3,4] [expert consensus].' Unclear: what is meant by national clinical guidance based on AMR patterns … Community = outpatients? Please clarify
Healthcare	General comment: the list of elements is very ambitious, I suggest a ranking for what is absolutely necessary and how to start
Laboratories	'Ensure that susceptibility testing and reporting are in accordance with treatment guidelines (selective reporting), and European and national standards [expert consensus]. Example: Selective reporting for urinary tract infections' Refer to EUCAST (methods, breakpoints and reporting)
Prescribers	What is a 'prescriber' and what is a 'community'? the community recommendations also address a prescriber Please clarify Overall the section is the content for a prescribers' (advanced) training programme Possible the section a may be shortened a little bit and more to the point
Prescribers	'if antimicrobial treatment is not considered necessary, give patients advice about the expected natural history of the illness, the limited or absent benefit of antimicrobial treatment, and the potential unwanted side-effects of antimicrobials such as diarrhoea and rash, as well as advice about actions in case of worsening clinical condition (safety netting)' The sentence is enigmatic - what is a appropriate safety netting? Probably to spare AB may not be possible to all patients Please clarify.
Pharmacists	Question: This section refers to pharmacists in the community setting only? So it is Pharmacists and pharmacies
Nurses	The implication of nurses is extremely important to endorse prudent use of AB More details – some issues from the prescribers?
Public, patients	Too much dont's, again this is content of information programs for the public Rephrase as Positive sentences: Only use antimicrobials when prescribed by a doctors or a medical institution Use antimicrobials as prescribed by your doctor or your institution If you have questions ask the doctor, nurse, pharmacist, hotline … Do not stop or change the doses of antibiotics without asking your doctor, institution or pharmacist.
Clinical microbiologist (Sweden)	

Section of document	Comment and rationale – proposed change
National and regional	'Explore incentive systems for appropriate prescribing [expert consensus] [9]. Examples: Introduction of appropriate prescribing as a certification indicator for healthcare facilities and Pay for Performance (P4P) in primary care (France), antibiotic quality premium (NHS England) [2]' I believe that the point is incredibly important, but I think that exploring financial incentives for prudent antibiotic use should not be limited to prescribers, but include all stakeholders, warranted that everyone can agree on one or more common objective indicator reflecting prudent use.
Healthcare facilities	I believe that it could be clarified that antimicrobial stewardship programmes should target individual assessment of patients with suspected infections as well as general guidelines, but not merely general guidelines.
Healthcare facilities	I believe that the availability of timely investigations of suspected antibiotic allergy should be a part of the one health perspective of prudent antibiotic use. The addition of such a comment could be considered
Prescribers	'reassess antimicrobial treatment and consider modification (e.g. de-escalation, discontinuation or switch to oral treatment) after 48–72 hours in hospitals, and in specific circumstances in other settings according to guidelines' I believe that hospitals should consider taking a structured approach to 'wait-and-see' situations in patients with no signs of severe infection but where it is simply unclear whether the patient's current illness would benefit from antimicrobial treatment. Whether we like it or not, this is a very common clinical problem. The addition of a comment regarding this could be considered
Research	Since present antibiotics, however prudently used, as well as novel antibiotics, however needed, will all promote selection pressure, it may be mentioned that research exploring non-antibiotic ways to treat infections should be promoted.
Paediatric infectious diseases specialist (Spain)	
National	The EU Commission should consider Mandatory for countries to have a budgeted plan, with clear specification for each action at different levels, including each institution It is a key point to have the appropriate budget to achieve the objectives of this strategic plan
Healthcare facility	Stewardship committee should include a member of the hospital (institution) board that may be the responsible for the appropriate development, initiation and functioning of the stewardship program of the institution. This member would directly report to the board about the activities and results of the program, and assure that the budget to carry it out is appropriate
Healthcare facility	An Infectious Disease Pediatrician should be part of the antimicrobial stewardship team due to: - Very specific conditions of this population in terms of diseases, pharmacokinetics, dosage of antimicrobials, adverse events and, even, efficacy of therapy - Age as an important factor related to infectious diseases and therapy, including newborns and premature babies
Indicators	- For pediatrics, DDD is not a useful indicator of prescription due to a variation of dose according to weight or body surface. Probably, the most standardized way to measure antimicrobial consumption would be days of therapy (DOT) per 100 patient-day - E.G., an useful indicator in pediatrics may be proportion of children > 3 months of age without risk factors discharged on antibiotics from the Emergency Room - *C. difficile* infection is difficult to quantified in pediatrics due to high rate of colonization, especially in young ages
Healthcare facility	Rapid and/or point-of-care diagnostic tools have demonstrated a decrease in antimicrobial prescription in children. Furthermore, the importance of several of these diagnostic tools may be different between children and adults, thus their importance may also be different. For example, some very important ones in pediatrics may be group A Streptococcus rapid test from pharyngeal samples or respiratory viruses rapid test from nasopharynx
Healthcare facility	Specific information and considerations for pediatricians should be including. Some examples may be: - Resistances. Usually very different compared to the adult population, in part for a different use of antimicrobials in children - Pharmacokinetics. Completely different in children vs adults. Important point for research (see below). - Guidelines are very different and, although many adults guidelines cover some aspects of the pediatric population, in general, this information is clearly incomplete and inappropriate for the optimal approach to infectious diseases in children
Healthcare facility	Susceptibility reports should be disclosed and discussed by the Microbiology Service with certain frequency, e.g., every 6 or 12 months. These reports should include pediatrics in a separate report and its specific units (Intensive Care, Neonates, Hematology-oncology, Surgery, etc). Frequently, the susceptibilities patterns of various units are different even though they may be closely situated, in part related to its functioning as closed compartments (different patients, different personnel, etc)
Nurses	Keep in mind that in some countries (for example, Spain) nurses do not prescribe.
Healthcare facility	For a successful implementation of the programs the collaboration and implication of personnel from key units (such as intensive care) are extremely important. This would include physicians and nurses, among others. These individuals could participate in educational activities and may be an example to their partners to modify conducts that, ultimately, would optimize the antimicrobial use
Education	Promote educational activities and training among different institutions (primary care, hospital, etc). Since people move freely between the community and healthcare institutions, shared or common activities or strategies may be important between, e.g., hospitals and primary care centers
Research	It is extremely important to promote research in pediatrics since it is a specific population with very specific characteristics, as it has been mentioned above, and then, results obtained in adult studies frequently do not apply to children Public institutions (at different levels; e.g. hospital, primary care) should be implicated in developing and supporting research in antimicrobial stewardship.
Fellow, Global Health and Tropical Medicine (Portugal)	
Healthcare facilities	The microbiology laboratory plays an important role in antimicrobial resistance prevention and control since its work is fundamental for identify antimicrobial resistant isolates and can contribute to dose optimization based on data on minimum inhibitory concentration An antimicrobial stewardship team including at least a clinician (iii), a microbiologist and a pharmacist (iv).
Infectious Diseases/Intensive Care specialist (France)	
Introduction	The definition of antimicrobial resistance proposed is quite restrictive, as it only includes acquired resistance: In most textbook, antimicrobial resistance also applies for constitutive resistance (e.g. E. coli are all resistant to vancomycin) Either you indicate that the definition provided is 'acquired antimicrobial resistance', either you detail the two situations (constitutive, or acquired resistance)

Section of document	Comment and rationale – proposed change
	Definition of antimicrobial therapy: The accurate contrary of 'empiric' is 'documented', not 'definitive': Many empirical treatment turns out to become 'definitive', if they are effective and no additional documentation is obtained Substitute 'documented' for 'definitive'
Prescribers	'for a patient with sepsis, start antimicrobial treatment via the intravenous route within 1 hour of 173 recognition of sepsis' Definition of 'Sepsis' has been recently changed (Singer M et al. JAMA 2016). Your recommendation that patients with sepsis should receive iv ATB within one hour is only valid with the new definition (i.e. Sepsis = life-threatening organ dysfunction caused by a dysregulated host response to infection), not with the one you refer to (Dellinger RP et al. Intensive Care Med 2012). Otherwise, your statement will lead to an excess of inappropriate ATB. Change the reference (28) to Singer et al. JAMA 2016), and indicate what is the new definition of sepsis (see the previous column)
Hospital pharmacist (Malta)	
Title	The EC (and WHO) is aiming at ONE HEALTH, so the title might be misleading EU guidelines on the prudent use of antimicrobials in human medicine as part of the One-Health initiative
Intro	'Combined with the meagre development of novel antimicrobials, the spread of resistance to existing ones is leading to loss of effective options for the treatment and prevention of infections, representing a health security threat for Europe' Threat not only for Europe Text to be amended to mention Global effect but also alluding to the ECDC remit only within EU...
Definitions	'Prudent or appropriate antimicrobial use…' Cite other alternative names: Judicious; Rational; Adequate; Correct; Optimal...
Definitions	'Antimicrobial stewardship' Antimicrobial vs Antibiotic. Most Stewardship programmes mainly (if not exclusively) refer to antibiotic (antibacterial) This should be clarified that the terms can be used interchangeably or that antibiotic stewardship is often the major component...
Purpose	Change 'Antibacterials' with 'Antibacterial agents'
International	'Scientific societies should support the development of good clinical practice guidelines that are adaptable to local resistance patterns and address the most common infections [expert consensus].' Apart from local AMR formulary needs to be considered These guidelines should reflect drugs licensed in the respective member state.
National and regional	At the local/national level should other stakeholders: regulators (e.g Medicines Agencies) and payers (e.g. insurance) and policymakers be addressed/included in more detail?
National and regional	'Fund, develop and implement a national action plan for appropriate use of antimicrobials in human medicine including multi-faceted interventions adapted to local conditions [1] [expert consensus].' Add: as part of a One-Health NAP...
National and regional	Some of these functions may be desirable but not feasible (eg pack size if dispensing by unit is not ideal; also where there is no knowledge of indication and prescription but overall consumption some functions are not feasible To add a proviso at the end
Prescribers	Should one mention the importance of appropriate sampling for C&S before starting antimicrobial agents in septic patients? (mentioned later) Suggest including this ALSO here.
Prescribers	Regarding 'avoid treatment for colonisation without evidence of infection [29] [expert consensus]' Mupirocin nasal decolonisation should be mentioned as an exception, right?
Prescribers	Regarding 'inform the patient about their antimicrobial treatment' In the ICU the patient is often sedated This applies only if patient is conscious with a GCS of 15?
Pharmaceutical industry	Regarding 'Ensure that promotional activities are in accordance with the summaries of product characteristics (SPCs) and national guidelines, and that they mention the risks of antimicrobial resistance and inappropriate use [expert consensus]', some drugs are recommended at a higher dose than the SPC (eg colistin for CRE). To clarify that in certain situations eg tx of MDRO a higher dose than that recommended on the SPC might be recommended locally by the local guidelines. The Pharma Industry could/should/would be aware of this...
Appendix 2	'Proportion of cases of Staphylococcus aureus bacteraemia where infectious disease consultation was provided' What about clinical microbiologists? maybe change to ID or CM
Appendix 2	'Proportion of combination treatments among total number of antimicrobial treatments' It is important to compare with local guidelines for each indication. So e.g. a low % combo for CAP where the guidelines recommend a beta-lactam + macrolides would be 'inappropriately low' but if the guidelines recommend monotherapy, then a low % of combo would be 'appropriately low'. Text to include a mention of different diagnoses/indications and respective local recommendations. Otherwise the indicator would give irrelevant benchmarking and/or information...