Meeting Report

WHO Informal Consultation on options to improve regulatory preparedness to address public health emergencies

Geneva, Switzerland

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Abstract

The recent Ebola crisis in West Africa highlighted a number of major regulatory shortcomings in the world’s preparedness for public health emergencies. Although National Regulatory Authorities (NRAs) have a key role to play, many lack capacity and resources and have no effective preparedness and response plans in place. In May 2017, WHO held an informal consultation on options to improve regulatory preparedness to address public health emergencies covering in vitro diagnostics, therapeutics and vaccines. It was attended by regulators from both high-income countries (HICs) and low- and middle-income countries (LMICs) as well as manufacturers, subject matter experts and other stakeholders. The meeting reviewed available regulatory tools and pathways, including the WHO Emergency Use Assessment and Listing process (EUAL), as well as regulatory collaboration arrangements between countries and capacity building activities. A number of recommendations for moving this agenda forward were made on which WHO will now reflect with a view to developing an action plan based on priorities and available resources.

1. Introduction

A plenary session at the International Conference of Drug Regulatory Authorities (ICDRA) held in South Africa in 2016 reflected on the lessons learned from the Ebola outbreak in West Africa as well as the ongoing public health response to the Zika virus epidemic (1) and identified a number of key regulatory gaps. First, many National Regulatory Authorities (NRAs) remain unprepared to face a public health emergency. The point was powerfully made that any country could find itself involved in a public health emergency and having to put emergency regulatory processes in place in the heat of the moment only adds to the difficulties of an already difficult situation. A second key gap is the weakness of drug regulatory systems and lack of capacity in many LMICs. NRAs do not always have the resources, expertise or support they need to do their job properly. Compounding this problem, many candidate products that are developed to address public health emergencies are at the cutting edge of science, sometimes from small companies with little regulatory experience, and are a challenge for even the best-resourced and most experienced NRAs to evaluate. A third key gap is that many NRAs have limited capacity and experience of communicating effectively with stakeholders, particularly the media and public. This led, for example, to one clinical trial for an Ebola vaccine candidate being halted in one country because of adverse publicity directed against the NRA for authorizing the trial to take place.

An R & D Blueprint for action to prevent epidemics, published by the World Health Organization (WHO) in May 2016 (http://www.who.int/blueprint/about/r_d_blueprint_plan_of_action.pdf?ua=1) provided an overview of key issues to be addressed and a plan of action. In February 2017, the WHO R & D Blueprint Scientific Advisory Group (SAG) proposed that a consultation be convened on options for regulatory pathways for products for priority pathogens in emergency and non-emergency settings and that the consultation covers vaccines, diagnostics and therapeutics. It also proposed that the consultation
should include a review of the WHO Emergency Use Approval and Listing (EUAL) process.

To address the recommendations made to WHO by ICDRA and the R & D Blueprint SAG, the WHO held a consultation in Geneva on 17-19 May 2017 to consider options to improve regulatory preparedness to address public health emergencies. The meeting was attended by regulators from both HICs and LMICs, vaccine and diagnostic developers, funders and other stakeholders and subject matter experts. The objectives of the meeting were to review available regulatory tools and pathways and see what else may be needed to improve regulatory preparedness to address public health emergencies. This would include identifying appropriate fora for dialogue on regulatory pathways, vaccine platform technologies and novel clinical trial designs for products against emerging infectious disease pathogens. Also, it was an opportunity to consider the need for further review and development of the WHO Emergency Use Assessment and Listing (EUAL) process which has only relatively recently been established through the WHO Prequalification programme.

2. Setting the scene

The meeting heard of a low-income country regulator’s experience during two public health emergencies, H1N1 in 2009/2010 and Ebola in 2014/1015, which highlighted several concerns common to NRAs in many LMICs. These included limited NRA capacity and experience, poor information sharing by stakeholders and, especially, lack of specific provisions or procedures for dealing with regulatory issues during a public health emergency. Ethical issues were also discussed in the light of the Ebola crisis, including ethical review of research, early data sharing versus data protection, and the movement of biological samples across national borders. The challenges with biological samples included ownership, use of the sample in the future as well as the need to get the sample to an appropriate laboratory efficiently. It was important to understand the problems that needed addressing to get the right products to the right population / patients at the right time with the best understanding possible of how to use the products most safely and most effectively. In particular, there was a need to facilitate the use of products which might not be licensed during an emergency but with the benefit of appropriate regulatory oversight and communication with patients and practitioners about the level of knowledge that exists about the product. The importance of regulatory oversight and appropriate communication should be made clear as well as how they facilitate the best public health decision-making during a public health emergency. In a poorly regulated environment, a public health emergency may open the door to dubious remedies and could allow the unscrupulous to take advantage of the very vulnerable through substandard and/or falsified products.

3. Review of mechanisms providing access to investigational products under a public health emergency

Despite the challenges facing regulators during times of public health emergencies, especially in LMICs, important developments are taking place that should strengthen the preparedness and response of regulators to such emergencies. One of these is the WHO Emergency Use Assessment and Listing (EUAL) mechanism developed in response to the 2014 - 2016 Ebola outbreak, the details of which were explained.
The EUAL is a risk-based approach designed to serve as an accelerated procedure for assessing and listing candidate in vitro diagnostics (IVDs), therapeutics and vaccines for use during public health emergencies. The procedure has three key components: review of the documentation relating to the manufacture of the product, including compliance with WHO manufacturing quality norms and standards, review of documentation relating to safety and efficacy/performance, especially with respect to use in the area of the public health emergency; and, where applicable for diagnostics, an independent laboratory evaluation, coordinated by WHO, of the product’s performance and operational characteristics.

Some regulatory agencies already have various regulatory processes in place for authorizing the use of investigational medicinal products during emergency situations. The US FDA, for example, reported that it has a process called Emergency Use Authorization (EUA). This permits the FDA to authorize the emergency use of an unapproved medical product or an unapproved use of an approved medical product. Making an investigational vaccine available to persons at risk from the emergent disease under an EUA would require a determination by the Secretary of HHS of a public health emergency or a significant potential for a public health emergency that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad. Certain criteria for issuance of an EUA must be met. Informed consent and ethics review are not required. However, to the extent practicable under the emergency circumstances, authorization for use should include conditions to protect recipients. Recipients must have an opportunity to accept or refuse the EUA product and must be informed of any consequences of refusing administration of the product. Data would have to be provided to show that the product may be effective and that the known and potential benefits outweigh the known and potential risks.

Access to investigational products can also be made under FDA’s Expanded Access Provisions where again there are strict criteria to be met, including that no satisfactory alternative is available. FDA’s Expanded Access provisions (21 CFR 312 Subpart I) are intended to facilitate access to investigational drugs for patients with serious or immediately life-threatening diseases or conditions when there is no comparable or satisfactory alternative. The primary purpose is to treat the patient’s disease or condition, not to obtain information about the safety or effectiveness of a drug. The requirements for making a vaccine available under the expanded access provisions are similar to those for an IND clinical trial but there is potential for wider use if certain criteria are met (e.g. sufficient evidence of safety and effectiveness to support the expanded access use).

The European Medicines Agency (EMA) explained that it also has a number of regulatory tools in place for rapid decision making and product authorization on the basis of less comprehensive data in the event of a public health emergency. These include conditional marketing authorization and market authorization under exceptional circumstance where, for example, comprehensive data may not even be possible. The former is valid for only one year. Neither requires the declaration of a public health emergency, but can be used in such circumstances. The EMA can also use Article 58 to give a scientific opinion in the context of cooperation with the WHO in the evaluation of certain medicinal products for human use exclusively outside the
EU. The rolling review principles are much used in such circumstances, where data are evaluated as they become available. Again, use of Article 58 does not require the declaration of a public health emergency; however, it can be used under such circumstances.

Health Canada described several pathways it has available to provide access to much needed medical products in emergency situations. These include a Special Access Programme and the use of Interim Orders which enable the Minister of Health to implement new regulations in cases where immediate action is required to deal with a significant risk to health, safety or the environment. In addition, an expedited review procedure is available as also is the more recent Extraordinary Use New Drug (EUND) regulatory pathway. The latter pathway provides a mechanism for authorization of medical products based on non-clinical and limited clinical information. However, candidates are expected to meet standard quality and GMP requirements. For these pathways there are enhanced post-market requirements and a post market plan is required. EUND approved products are restricted to government use, for example use by the Public Health Agency of Canada. New measures are under consideration for blood which includes importation of material such as convalescent plasma collected as per WHO guidelines to treat Ebola infection. The importation of other drugs for urgent public health need is a new pathway that would allow for the importation of a product included on a list of drugs for urgent public health use. Drugs will have had to have been authorized for sale in the USA, the European Union, or Switzerland for use in the same urgent public health need.

4. Review of the WHO EUAL Process

The meeting reviewed the WHO EUAL process in the three product lines and noted the successful use of the process and the challenges encountered.

4.1 WHO EUAL for diagnostics

It was reported that to date WHO had received 25 applications for EUAL for IVDs for Ebola assays, 7 of which were successfully listed under the EUAL process as eligible for WHO procurement with the EUAL caveats. Thirty three applications for EUAL had been received for Zika assays, only two of which were EUAL listed as eligible for WHO procurement with the EUAL caveats. There was therefore more success in the Ebola than in Zika field, but several challenges were identified. These included poor quality of submissions and assay validation data, the lack of standards, reference preparations and samples for validating assays, including ethical clearance related to the sourcing of these materials and concerns about the biosafety of these diagnostic tests. From the perspective of manufacturers and regulators there was a need for better guidance on laboratory studies required for IVDs in the EUAL process, as well as the availability of international reference materials.

4.2 WHO EUAL for vaccines
The meeting heard that two manufacturers had submitted EUAL applications for candidate vaccines using a rolling submission approach and that the submitted data are being reviewed. One submission was for the rVSV-ZEBOV-GP Ebola vaccine and the other for the prime boost Ebola vaccine Ad26.ZEBOV/MVA-BN-Filo. More data are expected by the end of 2017 and in both cases, updated benefit-risk analyses are being performed regularly. However, because the WHO lifted the Public Health Emergency of International Concern for both Ebola and Zika, no further submissions to the EUAL process for these diseases can be accepted.

From a product developers’ perspective, there was a need to simplify and revise the EUAL process for vaccines and to improve clarity on procedural aspects whilst avoiding overlap with the function of NRAs, for example in pharmacovigilance.

4.3 WHO EUAL for therapeutics and biotherapeutics including convalescent plasma

There were only 4 priority products for consideration under the EUAL process in this group, which includes convalescent plasma, and none of these had proceeded far enough to justify EUAL submission. There is therefore no experience of EUAL for medicines and no EUAL was issued for any therapeutic during the Ebola outbreak.

4.4 Future options for WHO EUAL

A general discussion of the EUAL process identified several issues which needed attention and the meeting made several recommendations for consideration by the WHO. First and foremost it was considered that WHO needed to clarify aspects of the current EUAL procedure. Indeed, it was suggested that WHO should change the name of the process from “Emergency Use Assessment and Listing” process (“EUAL”) to “Emergency Use Listing” process (“EUL”) since in the EUAL acronym the ‘A’ is not well understood. Many equate “A” with ‘authorization’ as in the U.S. FDA Emergency Use Authorization (“EUA”) process. It should be made clear that the EUAL process should be used only in exceptional circumstances and not in every outbreak or during initial response to an outbreak, if other licensed or standard modes of therapy are available. Primarily, it should be used at the declaration of a Public Health Emergency of International Concern, as is the current requirement, but the consultation believed it could also be used in other public health emergencies, if appropriate. Recommendations to use an investigational product outside of a clinical trial setting under the EUAL framework should be based on pre-determined rationale or criteria (so as to avoid decisions based simply on hope or political pressure) that include: (1) the preponderance of scientific evidence to suggest the product will be beneficial and its use outweighs the known risks, (2) product development is underway and access outside of the clinical trial will not interfere with its progress, and (3) supplies are sufficient to meet the public health need outside the clinical trial setting. Such use outside a clinical trial setting might include use in first responders and mass distribution in an area, if such was considered the most appropriate public health response by the responsible public health officials. How the EUAL process relies on assessment already performed by NRAs should be made clear. In addition, WHO should clarify the relationship of the EUAL process to activities at the NRA level and explain how the EUAL may be used by NRAs and procurers in their decision-making. There should be timely communication of any potential decision with regulators, especially those in potentially affected countries or regions, prior to
any announcement. This can be done via conference calls and communication tools such as talking points and/or Q&As. In collaboration with NRAs, WHO should develop or recommend a common template for EUAL application that can be used for both WHO and NRA applications for emergency use.

The meeting also recommended that WHO institute a pre-EUAL submission process to obtain, maintain, and evaluate, in an on-going manner, available data to better prepare to make a EUAL listing decision as quickly as possible once a public health emergency occurs and the context in which the product might be used is known. Pre-EUAL submissions should be limited to potential use to combat certain priority pathogens or situations outlined in the WHO R&D Blueprint and applied only to unlicensed new or repurposed products. In addition to data collection on product quality, safety and efficacy, the meeting considered that several other matters should be addressed as part of this new pre-EUAL process. These include: i. the need for any new physical standards, guidelines, companion diagnostics or other normative guidance. ii. plans for (as appropriate): clinical trials (with possible pre-approval by the responsible NRAs and ethics committees/boards), use in first responders, in health care workers, and/or in wider populations, iii. interactions with potentially affected NRAs; plans for collecting, saving, transporting, and/or exporting any biological samples if used under a future EUAL; and communication and pharmacovigilance plans if used under a future EUAL. It was important also that WHO should ensure that relevant pre-EUAL submission information and other relevant information developed during the emergency can be shared with relevant NRAs and ethics committees/boards. This could be accomplished by establishing mechanisms for sharing such data before the need for a specific EUAL and by developing (or recommending) a common template for data submission so that data can be easily shared with NRAs and ethics committees/boards.

5. Norms and standards for countermeasures for emerging infectious diseases

The meeting noted that WHO had a key and longstanding role in developing, establishing and promoting international standards with respect to biological and pharmaceutical products used in human medicine. This included WHO Biological Reference Materials used to standardize biological products and assays as well as WHO guidelines and recommendations on the quality, safety and efficacy of vaccines and biotherapeutics. These norms and standards assist both the WHO prequalification programme and WHO Member States in the evaluation and on-going quality control of biological and other medicines and related in vitro biological diagnostic tests.

It was reported that numerous WHO guidelines are available on the quality, safety and efficacy of vaccines and biotherapeutics. These form the basis of many national requirements and of both routine prequalification listing decisions and the EUAL evaluation. Guidelines on regulatory preparedness for human pandemic influenza vaccines (2) were adopted by the WHO Expert Committee on Biological Standardization (ECBS) in 2007 which, in 2016, were complemented by guidelines on regulatory preparedness for the provision of marketing authorization of human pandemic influenza vaccines specifically in non-vaccine-producing countries (3). Progress made with the development of Guidelines on the quality, safety, and efficacy of Ebola vaccines was discussed. This document was adopted by the ECBS
in October 2017. The Guidelines focus on vaccines based on viral vectors, as these are the vaccines currently at the most advanced stages of development. For the first time in any WHO guidelines of this type, opportunities for accelerating product development and availability during a public health emergency are also discussed, including novel clinical trial designs, with the intention of facilitating progress towards licensure. However, the guidelines do not discuss regulatory pathways for approving investigational vaccines for use in public health emergencies. Such pathways are often NRA specific and the issue is being addressed separately. In response to the Ebola outbreak, guidance on managing ethical issues in infectious disease outbreaks and on good participatory practice for clinical trials involving emerging pathogens had also been developed by the WHO. Guidance on some of these issues is also available from regulatory authorities such as the US FDA and the EMA, as well as from the International Conference on Harmonisation (ICH).

The availability of international reference preparations and panels in support of product validation and on-going quality control is an important aspect of assuring product quality, safety and efficacy. The meeting heard that work on WHO International Biological Standards, reference materials and panels for IVDs used in diagnosing priority pathogens, as well as in assays to measure antibody responses to candidate vaccines, was progressing and a number of reference preparations and panels had already been established for Ebola and Zika assays by the WHO ECBS (http://www.who.int/bloodproducts/catalogue/en/). This work is resource intensive and technically demanding and had experienced a number of challenges including the sourcing of candidate materials. No global system was in place to expedite this in times of emergency, but attention was drawn to the implications of the Nagoya Protocol (https://www.cbd.int/abs/). The Nagoya Protocol is a treaty under the Convention on Biological Diversity, which governs the international sharing of genetic resources (e.g. plants, animals, microbes) to promote the fair and equitable sharing of benefits that arise from the use of genetic resources. While the Nagoya Protocol sets out broad principles, such as prior informed consent and mutually agreed terms, many national implementation decisions are left to parties to the treaty. Public health response to infectious diseases requires two equally important elements, rapid and comprehensive sharing of pathogens and equitable access to diagnostics, vaccines and therapeutics. The Nagoya Protocol supports access and establishes a more equitable approach for sharing benefits but there are concerns that its implementation could slow down or limit pathogen sharing. This is due to the complexity of varying domestic implementation of legislation. It has so far been discussed from the perspective of the pandemic influenza preparedness framework (A70/57 WHA 2017). Platform systems for producing some reference reagents for diagnostic assays were under development. For example, a PCR standard using an HIV backbone to package pathogen RNA sequences in a virus like particle had been successfully used to develop Ebola reference reagents. These synthetic viruses were safe, non-replicative, non-infectious as well as easy and fast to produce. Antibody standards using pseudo-typed viruses were also being developed for use in assays to measure antibody for vaccine efficacy assessment. With respect to the process of establishing WHO reference materials, there would need to be some flexibility in the ECBS process to accommodate emergency situations, such as the establishment of interim standards in the case of priority pathogens of public health potential.
The meeting considered that WHO should continue developing measurement (physical) and written standards (guidelines) that serve as a basis for world-wide regulatory evaluation, PQ, and EUAL, taking into consideration: 1) priority pathogens defined by the R & D Blueprint or subsequently agreed with WHO and 2) a more flexible and dynamic approach to developing and establishing standards for quality, safety and efficacy of products for use in public health emergencies. It was considered that collaboration with the Coalition for Epidemic Preparedness Innovations (CEPI) and other partners is critical for a coordinated and timely outcome at the global level.

6. Safety and vigilance for emergency use products

Several participants spoke about the need for timely collection of safety information on vaccines and therapeutics used under emergency access situations, despite the difficulties that the emergency situation might present, in order to safeguard recipients and to inform public health decisions. The level of prior knowledge on the safety of such products is likely to be variable but generally limited for emerging pathogens. Knowledge from use of similar product constructs for other diseases will be highly supportive but cannot replace the need to properly profile safety of the actual products in the emergency setting. Safety concerns and uncertainties should be balanced against the proven and expected benefits for regulatory decisions for clinical trials approvals and for potential authorisation in emergency settings. Both the EMA and US FDA mentioned the enhanced pharmacovigilance plans put in place for the use of the H1N1 and other pandemic influenza vaccines. The need for increased collaboration and the sharing of preliminary data among disease control programmes, public health agencies, and regulators during an emergency situation was emphasised. However, other participants pointed out that these frameworks may not always work in the resource limited settings of LMICs where often there was no appropriate law on pharmacovigilance or the systems maybe fragmented or quite minimal. Discussion raised two key concepts; the importance of networking and the need to strengthen pharmacovigilance systems in LMIC settings. In networking, it was important to improve coordination between the NRA, public health programmes and pharmacovigilance as well as Regional Committees, the appropriate WHO committees, such as the Global Advisory Committee on Vaccine Safety (GACVS) and the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP). Consideration should be given to sharing "confidential" data especially on safety and to facilitate inter-country collaboration. The strengthening of pharmacovigilance to deal with emergency situations should be seen as an opportunity to strengthen the pharmacovigilance system in countries as a whole. It was also essential that infrastructure strengthening should be part of regulatory preparedness plans and completed prior to another major public health emergency. In particular, LMICs needed support to develop skills and appropriate human resources to deal with the authorization of products for use in emergency situations.

7. Developing a consensus on options to improve regulatory preparedness

All participants agreed that mechanisms needed to be in place for reviewing and authorising the use of promising, but unlicensed, medicinal products within the shortest time frame possible in the event of a public health emergency. The meeting
heard that the experienced NRAs had several pathways in place for such an eventuality. It was believed that one size does not fit all and that a “toolbox” of pathways is needed with the flexibility to choose appropriate pathways based on context and in response to changing scenarios. The US FDA’s Animal Rule, which may provide evidence of the effectiveness of a vaccine or therapeutic product from animal studies, was one optional tool in circumstances where clinical trials are not feasible for one reason or another. The establishment of regulatory pathways for use in emergency situations should be part of national regulatory preparedness activities. While it was important for NRAs to prepare regulatory options for authorizing medicinal products during public health emergencies, there were other important actions which should also be considered. These included the formation of a network of NRAs where information could be rapidly shared under emergency situations. Several participants spoke of the benefits of collaboration between regulators during a public health emergency and strengthening regulatory collaborations and capacity were considered crucial, if not essential for LMIC NRAs. It was reported that excellent progress was being made by African regulators in this area through the establishment of the African Vaccine Regulatory Forum (AVAREF).

AVAREF was initially created by the WHO and African regulators in 2006 as an informal capacity building platform aimed at improving the regulatory oversight of interventional vaccine clinical trials being conducted in Africa. It has now expanded its membership of regulators and national ethics committee/board representatives from 23 to 54 African countries. It has also expanded its scope from vaccines to include other medicinal products and developed a system for joint reviews tested both in emergencies and non-emergency situations. The joint review process for parallel submissions of clinical trial applications, and for future approval of clinical trials, encourages harmonization of procedures and decision criteria and countries use the common report as the basis for their national decision currently. In addition, countries are encouraged to incorporate the regional processes into their national approach to clinical trial oversight. Regulators at the national level have different technical backgrounds, expertise and competencies but the system includes capacity building through direct and hands-on interaction with WHO and experienced regulators in Europe, Canada, and the USA. AVAREF is also involved in information sharing between countries during situations of public health emergencies, although there were legal aspects to be considered. It was recommended that WHO should map the current emergency provisions (regulatory and legislative) in LMICs and address legal or regulatory deficiencies that might prevent rapid implementation of any measures required to be implemented during an emergency. The meeting recommended that AVAREF guidelines and associated templates for expedited review of clinical trials (both by regulatory and ethics committees/boards) in the context of a public health emergency should be finalized and include provisions for including experts/NRAs from outside Africa as deemed appropriate in specific outbreaks. A table top exercise should be conducted to further inform the process and amend as necessary. WHO should consider exploring ‘mock-up’ practices for expedited review of candidate products on an annual basis with interested NRAs and ethics committees/boards.

Participants considered that the emergence and evolution of regulatory networks such as AVAREF and the International Coalition of Medicines Regulatory Authorities (ICMRA) will increasingly play an important role in building the capacity and
readiness of NRAs to deal effectively with public health emergencies. WHO should explore the use of other regional platforms and the feasibility of adapting models like AVAREF to other geographic areas to facilitate expedited regional assessment of clinical trials in the context of a public health emergency. The feasibility of a “diagnostics preparedness consortium” and measures to facilitate sample availability to support product development/product validation should also be explored by WHO.

The meeting noted that, in support of Member States, the WHO had developed the National Regulatory Authorities Global Benchmarking Tool (GBT) which provides an objective and well tested methodology for benchmarking regulatory systems, establishing an institutional development plan for addressing areas for improvement, and for monitoring progress. The tool also allows for an assessment of the maturity level of the regulatory agency/ system with the objective of bringing all regulatory authorities to a level commensurate with a well-functioning system, either through their own in-house capacity or through reliance on other agencies with an established appropriate maturity level. The tool comprises modules with indicators appropriate for most regulatory activities, including gauging the readiness and capacity of NRAs to deal with emergencies. It was considered that WHO should develop a clear set of expected minimum competencies that NRAs and ethics committees/boards should have for handling the emergency use of unlicensed medical products during a public health emergency. To support this work WHO should explore how these minimum competencies could be incorporated into the Global Benchmarking Tool (GBT) and supporting processes. WHO should also develop training modules and expertise verification mechanisms for NRAs and ethics committees/boards that wish to implement these competencies (using the Coalition of Interested Partners process) as well as define how they interface with International Health Regulations emergency competencies.

The meeting also recommended that WHO, in collaboration with experts on ethics, should develop guidance, on the procedures and pathways for the use of unlicensed medical products during a public health emergency and give guidance/assistance on when it is appropriate to use these procedures and pathways. Such guidance should include a glossary of various names of procedures and how WHO will use these terms. This could include: Emergency Use Listing (if that is the new name for the current EUAL procedure), Emergency Use Authorization, Conditional Approval, Accelerated Approval, Approval Under Special/Exceptional Circumstances, Expanded Access, Compassionate Use and so on. The guidance should include procedures for best communications practices (to the public, to practitioners, to government officials), for best pharmacovigilance practices, for best supply chain security practices, and for best continuity of business practices, in addition to unlicensed medical product assessment for access during an emergency.

8. Overall summary

Final discussion of meeting outcomes was conducted in a closed session, which also made recommendations to WHO. A summary of preliminary outcomes of the consultation is available on the WHO Essential Medicines website (http://www.who.int/medicines/news/2017/Preliminary_outcomes.pdf?ua=1). An important point made is that during the development of procedures to address access to unlicensed products in the context of public health emergencies, it is
imperative to involve national regulatory authorities, especially those from LMICs and those affected by the emergency. Also, when considering recommendations made by the consultation, WHO should ensure that there is appropriate participation and representation of all potentially affected NRAs. Furthermore, it was considered that effective emergency responsiveness from the less well-resourced NRAs will only be possible if current efforts to strengthen the NRAs of LMICs are supported and accelerated. WHO will now reflect on these outcomes and recommendations with a view towards developing an action plan based on priorities and available resources. It is clear that WHO resources, both human and financial, will need to be augmented for this purpose and discussion with collaborators and partners should be undertaken in the very near future.

References


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