

Viral Hepatitis Prevention Board

Vaccine shortages

LISBON, PORTUGAL

15 March 2018

Objective

To provide an overview of the current situation regarding hepatitis vaccine shortages and the role of the major stakeholders, and to elaborate a proposal for minimizing the impact on public health and ways to avoid future shortages by looking at

- the current hepatitis A and B vaccine supply constraints and the (potential) impact on public health;
- manufacturing, storage, quality and packaging issues that may influence availability;
- actions that are needed to avoid future vaccine shortages and to minimize the impact of hepatitis vaccine supply constraints on public health;
- the need for guidelines to prioritize the protection of those at highest risk during shortages and identification of bodies to produce and disseminate such guidelines;
- the different initiatives taken to prevent vaccine shortages or to minimize their impact; and
- lessons learnt.

Context

- Whereas the public health policy goal is to ensure a sustained, uninterrupted supply of affordable vaccines of assured quality, there have been regular shortages of several vaccines over several years globally, in developing and developed countries
- In addition to direct interruptions of the supply of hepatitis vaccines, shortages of other vaccines have been shown to affect on the situation for hepatitis A and B vaccines
- For public health programmes, market dynamics make it complicated at national and subnational levels to ensure sustained supplies of vaccines; authorities have to work with incomplete or absent data on supply and demand; balancing those requirements is essential to avoid shortages and stockouts
- For vaccine manufacturers, the issue of market dynamics is of great importance too, with the time-limited considerations of catch-up campaigns and the difficulties of markets for small-volume vaccines such as hepatitis A and monovalent hepatitis B

Context (continued)

- Manufacturers are hampered in anticipating necessary capacity by unpredictable demands, and cannot respond easily to shortages by rapidly producing vaccines (existing or new)
- Better data are needed on the economic impact and disease burden of epidemic outbreaks; another need is greater transparency about production capacity and other aspects of vaccine manufacture
- In conformity with EU competition law, however, exchange of information about product shortages (either at the manufacturing level or in the market) is prohibited when competitor companies are present in meetings: this might impede resolution of vaccine shortage
- Globally, many national problems have domestic causes, most frequently government funding delays; even if national problems do not result in disruptions at the national level, when they cascade down to district level the result is often that vaccination is disrupted

International context

- At United Nations level: Sustainable Development Goal 3: target 3.8 covers vaccines: “Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all”
- International and national action plans and programmes on vaccines: WHO’s Global Vaccine Action Plan 2011-2020 and the complementary European Vaccine Action Plan 2015-2020; WHO’s Vaccine Prequalification programme
- WHO’s governing bodies: in 2016 the World Health Assembly (in resolution WHA69.25) asked WHO to develop a global notification system for shortages of medicines and vaccines, urging Member States to implement effective notification systems and calling on manufacturers, wholesalers, global and regional procurement agencies and other relevant stakeholders to address the challenges of shortages and to participate in such notification systems
- In January 2018, WHO’s Executive Board recommended that at its session in May 2018 the World Health Assembly should call for the creation of a road map for WHO’s work on access to medicines and vaccines, covering the period 2019-2023

National contexts

- National Immunization Technical Advisory Groups (NITAGs) exist in many countries
- WHO in collaboration with the US Centers for Disease Control and Prevention (CDC) have developed training materials and regularly conduct training workshops on development of evidence-based recommendations in immunization policy and practice
- Some countries have elaborated national policy responses but there is a surprising lack of coordination and communication between concerned parties at supranational levels, including between the European Centre for Disease Prevention and Control (ECDC), the European Medicines Agency (EMA) and WHO
- CDC includes in its purchase contracts with vaccine manufacturers a requirement for them to provide CDC with advance notice of vaccine supply problems or disruptions, when possible, allowing anticipatory action; it consults regularly with stakeholders, maintains a website on vaccine shortages and disruptions, is authorized to implement controlled ordering of vaccines in case of shortages and can issue interim recommendations on vaccination schedules – examples of action in response to outbreaks of hepatitis A in 2017

Some major stakeholders

WHO, including headquarters and the Regional Office for Europe	Prequalification of vaccines; global and European vaccine action plans; proposed road map for programming WHO's work globally on access to medicines and vaccines; PAHO Revolving Fund for vaccines; working on a vaccine-shortage notification system; securing affordable supplies; collecting data on vaccine market, demand analysis, supplier base.
European Commission (EC): Directorate General for Health & Food Safety (DG Santé)	Enacts EC policies on public health, including vaccination; taken action to monitor shortages; issues European projects to handle vaccine issues (e.g. Joint action on vaccination)
European Medicines Agency	Taken action to monitor shortages; response from 2017 to hepatitis vaccine shortages; giving priority to unavailability/shortages of medicines (to 2020), including prevention of supply disruption and communication;

Some major stakeholders (continued)

European Centre for Disease Prevention and Control (ECDC)	Protects EU countries against infectious diseases; provides data and evidence for policy decision, strengthens public health systems, and supports responses to public health threats – independent assessments and options for vaccination policies
Other partners globally, such as CDC	Similar public health objectives
Health ministries and authorities, including NITAGs	Ministries set policy and enact legislation; NITAGs provide independent evidence-based advice to policy-makers and programme managers
Vaccines Europe, IFPMA and similar bodies	Trade associations supporting vaccines and industry
Other partners	Major donors, foundations etc (e.g. the GAVI Alliance, Bill & Melinda Gates Foundation); EASL, ELPA , VHPB, many more ...

Terminology

- There is a need for clear understanding of terms used – stockout, shortages
- WHO is reviewing terms and definitions in use, resulting in core definitions of shortage for application on the supply side and the demand side as well as for stockout (complete absence); in 2016 WHO issued report of meeting on definitions of shortages and stockouts
- The Seventy-first World Health Assembly in May 2018 is expected to request WHO to establish a global reporting system for notification of shortages (limited to products in the WHO Model List of Essential Medicines); to continue normative work relating to vaccines; and to support collaboration and training at all levels
- Without agreed and applied terminology, no reporting system will be relevant and useful

Causes of shortages

- The balancing act of vaccine supply and demand was clearly demonstrated to be much more complex than understood by even many health professionals; the range of factors underlying shortages and stockouts extends from production issues and limited supplier base to unpredictable and inflexible demand – they are exacerbated by limited communication between concerned parties.
- Many reasons have been advanced, ranging from sudden increases in demand (e.g. hepatitis A outbreaks, tenders, and new or modified national vaccination policies) to manufacturing problems and national and local issues such as poor forecasting and procurement, delayed funding, and poor stock management
- Incomplete data and lack of both transparency and open information exchange cloud the real reasons for the observed shortage in hepatitis A and B vaccines
- The vaccine manufacturing industry is alive to the issues and has extensively analysed the multiple causes
- Unpredictable demand is a consequence of a fragmented market, in which global production capacity (insofar as it is known) is not matched with demand from health ministries and the markets; data on demand are difficult to collate at supranational level (new recommendations, tender systems, ...)

Causes of shortages (continued)

- An industry working group has elaborated a series of detailed proposals, including:
 - action by the European Directorate for the Quality of Medicines & HealthCare to eliminate animal testing, optimize official medicines control laboratories and generally harmonize work across the EU (especially regulatory requirements and mutual recognition agreements),
 - learn lessons from countries that have introduced risk-based approaches to testing,
 - harmonize packaging and labelling requirements,
 - capitalize on the introduction of Datamatrix codes,
 - better anticipate demand, and
 - create a platform of regulatory and quality authorities for health authorities and vaccination providers
- The need for much better and broader communication of the issues involved to the public, politicians and health professionals was strongly underlined by all parties

Country experiences and impact

- A VHPB survey of vaccine shortages, among VHPB advisors, indicated in 13 out of 17 countries mainly in Europe, no substantial change in the situation since a previous survey in 2017: constraints on supply of hepatitis A and B vaccines continue, with country-specific challenges for hepatitis B vaccines
- Not all countries expressed a need for prioritization guidelines; some did and others had them prepared by their National Immunization Technical Advisory Groups (NITAGs)
- Shortages are being experienced, and are unpredictable; national agencies (mainly regulatory authorities) have responded variously, for instance by implementing systematic national monitoring and reporting activities
- Despite the consequent impact on immunization programmes, the limited data available indicate that the problem appears to be more logistical than one with public health consequences, but most countries do not investigate the vaccine-shortage problem and the experience of vaccination providers is not known; in low-prevalence European countries the chance of finding an acute case following a breakdown of vaccine supply is extremely low
- The effect of shortages and subsequent restrictions on vaccination will be tested by the occurrence of outbreaks and the consequences on herd immunity; in the case of illness that appears years after infection, the effect will not be seen for a long time
- In the USA, a federal country, CDC demonstrated how a publically-trusted organization responded successfully to large, multi-State outbreaks of hepatitis A that constrained supplies of vaccine: CDC deployed field teams, provided guidance, financial and laboratory support and policy development, liaised with manufacturers, introduced controls on ordering, and discussed dose-sparing policies for hepatitis A vaccine in controlling outbreaks

Some proposed responses

- Harmonization and mutual recognition of regulatory requirements and approval procedures for vaccines
- Possible establishment of a platform for national, European and US regulatory authorities, manufacturers and providers to exchange information
- Stockpiling of vaccines at the European level so as to ensure adequate response in case of outbreaks and emergencies
- Initiation of a reflection on whether outsourcing vaccine production and/or stockpiling, especially of low-volume products, to an oligopoly of manufacturing companies or nongovernmental organizations is fit for public health purposes

Recommendations

- In three words: ***surveillance*** (to detect shortages early in order to respond); ***coordination*** (between supranational and national organizations and all stakeholders); ***harmonization*** (definitions, regulations, guidelines and responses)
- A vaccine shortage and stockout reporting system is urgently needed at subnational, national, regional, European and global levels as a prerequisite for acting and solving the problems caused by disruptions in supply including the formulation and provision of guidance in cases of vaccine shortages or interruptions in or constraints on vaccine supply
- Ensure that any notification system and response to vaccine shortages are user-friendly for general practitioners, other vaccinating agents and vaccine recipients
- Capitalize on multiple national management capacities and approaches to compare outcomes and implement the best strategic approaches, based on data

Recommendations (continued)

- Key strategic directions are:
 - tackle the issues of vaccine shortages while conditions remain favourable, that is to say, now;
 - develop and implement a Global or at least a European vaccine shortage response mechanism – improving the predictability of demand and the response
- Pro-active actions:
 - *Short-term:* Change or prioritize recommendations at country level (with agreed and defined objectives); include more than one vaccine in a tender, if possible
 - *Long-term:* a possible consideration of storage and management of vaccines in case of shortages at central, regional or European levels
- Prioritization and management guidelines are a national responsibility, through the national immunization technical advisory group, as well as an issue at European and global levels
- VHPB should provide guidance on the management of shortages of hepatitis A and B vaccines in order to support hepatitis vaccination programmes. This guidance is requested to include prioritization and ways to adapt interim adaptations.

Recommendations (continued)

- Vaccine shortages and stockouts may be expected to occur and increase in the future. Outsourcing vaccine production from the public health responsibility to the global market economy has resulted in risks and constraints. Consideration should be given to ways in which the responsibilities of health ministries and vaccine manufacturers for prevention of disease and protection of the population can be shared.
- To facilitate that sharing of responsibilities, platforms should be established to bring together all stakeholders with the aim of balancing supply and demand predictions at national, European and global levels. There is a need for an organization to facilitate the creation of a venue for all stakeholders to launch the process. Objectives could be to design a platform for the exchange of comprehensive information and the short-term and long-term management of vaccine shortages on the basis of comprehensive data on manufacturing, stockpiling, logistics and regulations.
- A role for VHPB could be to raise awareness and urge the WHO Secretariat and WHO Member States to take action.