

## Perspectives on Quality

# Association of strategic management with vaccination in the terms of globalization

MIHAJLO RABRENOVIC<sup>1,2</sup>, MARIJA CUKANOVIC KARAVIDIC<sup>3</sup>,  
and IVANA STOSIC<sup>4</sup>

<sup>1</sup>Faculty of Business Economy and Entrepreneurship, Belgrade, Serbia, <sup>2</sup>Torlak' Institute of Virology, Vaccines and Sera, Belgrade, Serbia, <sup>3</sup>Faculty of Business Economy and Entrepreneurship, Belgrade, Serbia, and <sup>4</sup>Torlak' Institute of Virology, Vaccines and Sera, Faculty of Business Studies, Belgrade, Serbia

Address reprint requests to: Mihajlo Rabrenovic, Faculty of Business Economy and Entrepreneurship, 'Torlak' Institute of Virology, Vaccines and Sera, Belgrade, Serbia. Fax: +381-11-23-82-500; E-mail: mihajlo.rabrenovic@sbb.rs

Editorial Decision 11 December 2017; Accepted 16 January 2018

### Abstract

Globalization is having an ever growing impact on the field of vaccine production and distribution in the world and domestically. In this article we examine the impact of taking a strategic approach to vaccination programmes by all the relevant actors: WHO, UNICEF, national immunization programmes, and vaccine manufacturers and distributors. The review of the relevant literature indicates that there are commonalities to the worldwide vaccination programmes. A comparative analysis of various vaccination strategies recommended by WHO and the immunization calendars of certain European countries is made as well as an analysis of the Serbian vaccination programme. New and more expensive vaccines will continue to appear on the market in increasingly short periods of time.

**Key words:** vaccines, immunization, globalization, strategies, management, health

### Introduction

The management of vaccination strategies in a global market is growing in importance as new challenges arise. The development of new technologies, and business environment of the new age have resulted in the need for the application of strategic management [1] as a 'tool' which, in a swiftly changing environment, can help organizations achieve their objectives more efficiently and effectively by understanding their internal and external environments.

Globalization has enabled the free flow of resources, goods and workforce and may be perceived as one of the external environment factors impacting on the solutions for worldwide vaccination and the defined national strategies.

The World Health Organization—WHO [2] defines a vaccine as 'a biological preparation that improves immunity to a particular disease. The agent stimulates the body's immune system to recognize the agent as foreign, destroys it, and "remembers" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters'.

The vaccine manufacturing process itself is complex and varies from vaccine to vaccine.

In this article, we will examine the current state of vaccination and will project the future trends that may develop in the global and domestic vaccine market. We hypothesize that the application of strategic management approach increases the effectiveness and efficiency of organizations for vaccine production and distribution.

### Methods

The data has been obtained from sources such as literature review of the strategic documents of WHO, UNICEF, national vaccination calendars, reports by relevant European and national institutions, literature in the field of immunization, and relying on the legislation regulating this field.

Primarily, official resources at the national and international level have been used. This article is based on review of the previous research, statistic data, facts presented at the professional meetings,

etc. Collected data have been summarized and studied. In order to describe the subject of the research better, different immunization models have been presented by means of comparative analysis.

The author's aim was contribution to theory and practice to which the article refers.

## Results

Contemporary global trends dictate that vaccine manufacturers harmonize their production with the high standards of Good Manufacturing Practices (GMP). GMP is 'the aspect of quality assurance that ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the product specification' [3].

In the future, one can expect the further advancement of procedures in vaccine manufacture and distribution, and the upgrading of guidelines based on GMP and Good Distribution Practice (GDP) standards. The key issues that were found are as follows.

### Climate

There are specific challenges based on the climate zone of a particular country, i.e. regional distributors face various challenges in the delivery of vaccines, in the form of high or low external temperatures, the level of infrastructure development, access to locations that are hard to reach and without the necessary infrastructure.

### Changing environment

In the field of vaccine production, one requires standardization of processes and procedures with the upgrading of guidelines based on GMP and GDP.

The vaccine market is growing rapidly and there is increased investment in accelerated technological development, resulting in expensive vaccines. This is impacted on by the mergers of major pharmaceutical companies and a change in the type of vaccine needed for the young and the elderly.

### Role of organizations

WHO's and UNICEF's play an important part in the increasing vaccination coverage of the world population. The WHO guidelines provide the framework for national programmes and this determines the success rate of the programme by providing the standards to be attained.

To achieve this multinational companies deploy strategic management strategies to meet the needs of international programmes.

An evidence-based, cost-effective, safe and efficient immunization system is an integral part of a well-functioning health system [4].

### Local requirements

When planning the immunization schedule, each country should take into consideration the local epidemiological, programming and political situation, as well as the resources at its disposal [5]. Based on the data from Table 1, there is a noticeable trend of the constant introduction of new vaccines for the prevention of as many diseases as possible.

Parallel to the entry of new vaccines, there is the gradual cessation of administering vaccines against diseases which have been eradicated or are under control. For example, vaccine against tuberculosis (BCG) at birth, has been removed from the immunization calendar in

nine EU countries (Austria, Belgium, Denmark, Germany, Iceland, Italy, the Netherlands, Slovakia, Spain), while a number of member states administer it only to certain (at-risk) groups [6]. This is related to the risk profile of the population in each country.

For the purpose of making a comparison between the vaccination coverage in the Republic of Serbia to that in other countries, data of the WHO register has been accessed. The percentage of the BCG vaccination in the Republic of Serbia amounted to 99% (2011), 97.92 (2012) and 97% (2013) [7]. In view of the above-mentioned administration of vaccination against tuberculosis in immunization calendars in the countries referred to in Table 1, the comparison was made with the countries in the region, including Hungary, as one of the countries analysed.

The percentage of coverage in the countries of the region (Bosnia and Herzegovina, Montenegro, Macedonia, Croatia, Hungary, Bulgaria and Romania) ranged from 93 to 99% in the said period [7]. It can be concluded from the foregoing that Serbia's coverage corresponds to average values recorded in the region, where the vaccine against tuberculosis has remained in the compulsory immunization calendar.

An analysis of the lists of recommended vaccines for immunization by EU countries indicates that the introduction of new, polyvalent vaccines can be expected in the future, while at the same time certain specificities of national immunization policies will be maintained. The EU Council 'recognizes that immunization programmes require sustainable access to long-term funding and quality supply, and considers it necessary that policies to encourage vaccine research are supported within the Union, taking into account also the financial constraints, in order to make safer and more effective vaccines available' [4].

One can identify potential trends of further optimal evolution in Serbia pertaining to the introduction of the pneumococcal vaccine as being compulsory for the entire population (in accordance with WHO recommendations) and the introduction of the meningococcal vaccine in line with other European Union countries.

Keeping in mind the growth in dispersion of the HPV vaccine in Europe, together with application and the expansion dynamic in the European Union countries, we can expect this vaccine to be added to the Serbian immunization calendar in the coming years.

## Discussion

### Strategic approach to immunization

Given the importance the vaccination programmes, it is evident that a strategic management approach is an appropriate response to the challenges of global immunization, the World Health Organization and UNICEF developed the Global Immunization and Vision Strategy 2006–15 [8]. This joint document has 24 strategies divided into four strategic areas.

Beside the WHO and UN agencies, other vaccine market actors are also aware of the importance of a strategic approach to the vaccine process. According to some authors, the appropriate response is 'a challenge for policy makers and immunization stakeholders' [9].

Every country defines the immunization programme for its citizens depending on various factors—geographic location, economic parameters, population size, living conditions, cultural characteristics, etc. The competent national institutions determine the so-called 'immunization calendar', which encompasses a list of vaccines, the number of doses and the age at which each of the vaccines included is administered.

**Table 1** Comparative overview: vaccines for the compulsory immunization of children—WHO recommendation, EU countries and Serbia

Indication	WHO recommendation	United Kingdom	France	Germany	Italy	Czech Republic	Greece	Norway	Iceland	Hungary	Serbia
Tuberculosis	Specific groups	BCG	BCG	/	/	BCG	BCG	BCG	/	BCG	BCG
Hepatitis B	Hepatitis B	HepB	HepB	HepB	HepB	HepB	HepB	HepB	/	HepB	HepB
Polio	OPV + IPV or IPV/OPV sequential or IPV	IPV	IPV	IPV	IPV	IPV	IPV	IPV	IPV	IPV	IPV/OPV
Diphtheria	DTP	D	D	D, d	D, d	D	D, d	D, d	D, d	D, d	D, d
Tetanus		TT	TT	TT	TT	TT	TT	TT	TT	TT	TT
Pertussis		acP	acP	acP	acP	acP	acP	acP	acP	acP	acP
Haemophilus influenzae type b infection	Haemophilus influenzae type b	Hib	Hib	Hib	Hib	Hib	Hib	Hib	Hib	Hib	Hib
Pneumococcal disease	Pneumococcal (Conjugate)—PCV10 or PCV13	PCV13	PCV	PCV	PCV	PCV10	PCV	PCV13	PCV10	PCV13	PCV10
Rotavirus infection	Rotarix or RotaTeq	ROTA	ROTA	ROTA	ROTA	ROTA	ROTA	RV1	/	/	/
Measles	(Measles) MCV	MEAS	MEAS	MEAS	MEAS	MEAS	MEAS	MEAS	MEAS	MEAS	MEAS
Rubella	(Rubella) RCVs	RUBE	RUBE	RUBE	RUBE	RUBE	RUBE	RUBE	RUBE	RUBE	RUBE
Human papillomavirus infection	HPV for females aged 9–13 years	HPV for females	HPV for females	HPV for females	HPV for females	HPV for females	HPV for females	HPV for females	HPV for females	HPV2 for females	/

The vaccines included in national immunization programmes are listed in the table. Vaccines envisaged only for certain (specific) groups are marked as underline, while the data in italic (in the case of Czech Republic) refer to the vaccines which were recommended by the immunization calendar, but are covered by the budget.

According to UNICEF and WHO data, in 2013 there were 145 countries with a 3–5-year strategic national immunization plan. Among the 29 countries without multiyear national immunization plans included France, the country of traditional vaccine manufacturer Pasteur, as well as Germany and most Scandinavian countries.

For vaccines to arrive from the manufacturer to the end users safely and with undiminished quality, WHO has developed a group of guidelines called GDP, which are a logical extension of GMP.

The Vaccine Storage and Handling Toolkit [10] lists as important elements of the system the vaccine storage and handling protocols, a regular storage plan and a plan of action in the event of returning a lot or an emergency situation, staff (adequate number, expertise and training), equipment (measuring devices, temperature monitors, etc.) and equipment technical maintenance, strict temperature control, stock management, and the vaccine receipt and shipment procedures.

The application of strategic management is evident in the operational processes of global vaccine manufacturers and distributors who are significant vaccine market actors. This is key in ensuring that they can deliver on their ‘mission’ of ensuring the delivery of safe and effective vaccines and in investing efforts in the development and discovery of new vaccines. In this sense, the strategies applied by these companies in their organization focus predominantly on the ‘vision’ of creating a world devoid of diseases that can be prevented by vaccination.

**Globalization as a business factor**

The term globalization refers to the growth of mutual dependence between the markets of national states [1]. The globalization trend, initiated in the late 20th century, continues in the 21st century. It is a complex, multidimensional process present in all sectors of the economy and society. In that sense, its influence is visible in the production and distribution of vaccines as well.

The vaccine market has shown rapid growth in recent times; hence its value increased from five billion dollars in 2000 to almost 24 billion dollars in 2013, and is expected to reach 100 billion by 2025. WHO data indicates that five large multinational companies manufacture around 80% of global vaccine quantities [11]. Communicable diseases have become a global problem requiring a global response. As a result, there is a noticeable presence of globalization in the vaccine market and, this market will continue to attract investment in new technologies and new vaccines. The WHO states that, ‘the increasing globalization in the production and distribution of these biological medicines has opened new possibilities to better manage public health concerns, but has also raised questions about the equivalence and interchangeability of medicines procured across a variety of raw materials’ [12].

The Global Vaccine Action Plan (GVAP) constitutes the foundation of a legal framework for equal access to vaccines worldwide. The aim is to achieve the established goal of making vaccination coverage in every part of the world over 80% by 2020 [13].

Immunologists constantly face new challenges in the form of contributing to the eradication of known viruses, the development of new vaccines and a strategic approach to preserving and improving the population’s health. As a result of the noticeable increase in the number of cases of meningitis caused by *Haemophilus influenzae* among children in the 1970s and 1980s, a vaccine against this bacteria was developed and added to the immunization calendar by numerous countries [14]. In 1997, just 29 countries [15] included the Hib vaccine in their national

immunization programmes, whereas by 2014 this number had increased to 192 countries.

In Republic of Serbia in 2013, the Hib vaccination coverage amounted to 92%, which is slightly lower compared to other analysed countries in Table 1, where the vaccination coverage ranged from 94 to 99% with the exception of Iceland with 91% coverage reported for that year. With regard to the region, the average coverage is lower compared to the above-mentioned coverage in the countries referred to in Table 1, ranging from 87% (Bosnia and Herzegovina), 96% (Croatia) to 99% (Hungary) [7]. Nevertheless, according to the data in Table 3, the vaccination coverage in Serbia in 2015 testifies to the growing coverage trends in our country which correspond to the trends in the analysed European countries.

To prevent pertussis, i.e. whooping cough, all EU countries administer the acellular vaccine (acP). Poland has kept the whole cell vaccine (wCP) and the acellular variant is used only as the fifth dose [6]. It is interesting to note that vaccination against pertussis in Serbia used to be administrated using the combined DTP vaccine (Aldipete-T<sup>®</sup> by the Torlak Institute of Virology, Vaccines and Sera), which contains whole cell pertussis. The new Rulebook on Immunization and Manner of Protection with Medicines in Serbia came into force with effect from 1 January 2015, thereby launching the administration of the pentavalent vaccine within the compulsory immunization calendar, which also contains acellular pertussis.

Regardless of the vaccine form, all the countries referred to in Table 1 consider the administration of this vaccine one of the main vaccines in the compulsory vaccination programme.

In the analysis of the data from the WHO register for the period 2011–13 [7], it can be seen that Iceland had the lowest vaccination coverage of 91% (2013), whereas the coverage in other analysed countries in this 3-year period ranged between 95 and 99%. The DTP3 vaccine coverage in Serbia in 2013 was 95%, which is slightly lower than in other analysed countries having the following results: Germany and Great Britain 96%; Italy 97%; France, the Czech Republic and Hungary 99%.

The aforementioned vaccination coverage percentage in Serbia amounting to 95% in 2015, according to the data shown in Table 3, indicates a consistency in administration and the room for further coverage growth.

Table 2 is based on the WHO recommendations on the list of vaccines for children in certain regions, children in high-risk populations and children included in immunization programmes with certain characteristics. The recommendations mostly do not pertain to Europe; hence, we find few applications with the immunization programmes observed. The purpose of this overview is to provide a broader scope, which in globalization circumstances impacts the trends in the field of vaccination at a national level (in the analysed countries).

The herpes zoster vaccine is part of the programme in just three EU member countries: Austria, France, UK and the Czech Republic where it is registered but not yet available [6]. In this sense, one can expect the further expansion of administration of this vaccine in Europe.

The vaccine against hepatitis A is present in just five EU countries: Austria, Belgium and Cyprus for certain groups, the Czech Republic, and Greece for high-risk groups only [6]. Given that the WHO recommends the administering of this vaccine only to the high-risk population, the further trend of more and more countries adding this vaccine to their programmes for certain groups can be expected.

**Table 2** Comparative overview: vaccines for children in certain regions, in at-risk populations and included in immunization programmes with certain characteristics – WHO recommendation, EU countries and Serbia

Indication	WHO recommendation	United Kingdom	France	Germany	Italy	Czech Republic	Greece	Norway	Iceland	Hungary	Serbia
<b>For children in certain regions</b>											
Japanese encephalitis	Inact. Vero cell-derived/Live atten./Live recomb. Vacc.	/	/	/	/	/	/	/	/	/	/
Yellow fever	YF vaccine	/	/	/	/	/	/	/	/	/	/
Tick-Borne encephalitis	FSME-Immun&Encepur/TBE-Moscow&Encevir	/	/	/	/	TBE	/	/	/	/	/
<b>For children in some high-risk populations</b>											
Typhoid	Vi PS or Ty21a	/	/	/	/	/	/	/	/	/	/
Cholera	Ducoral (WC8S)/Sanchol&mORCVAX	/	/	/	/	/	/	/	/	/	/
Meningococcal disease	MenAMenC/Quadrivalent conj./Men. polysaccharide	MenC	MenC	MenC	MenC	MenB, MCV4	MenC, MCV4	/	MenC	/	Men A + C
Hepatitis A	Inactivated HAV/Live attenuated HAV	/	/	/	/	HepA	HepA	/	/	/	/
Rabies	CCVs (cell-culture-based vaccines)	/	/	/	/	/	/	/	/	/	/
<b>For children entitled to immunization programmes with certain characteristics</b>											
Mumps	Combined vaccine is recommended	MUMPS	MUMPS	MUMPS	MUMPS	MUMPS	MUMPS	MUMPS	MUMPS	MUMPS	MUMPS
Influenza	Children aged 6–59 months	TIV/LAIV	/	/	/	TIV	TIV	/	/	/	/
Varicella	Varicella	VAR	/	VAR	VAR	VAR	VAR	/	/	/	/

Source: WHO, ECDC, EFZO (2014, 2015, 2016).

**Table 3.** Coverage of vaccination in the Republic of Serbia in 2015

Age of the vaccinated and type of vaccine	Coverage (%)
At birth	
BCG	98.28
At age 1	
DTP3/DTaP-IPV-Hib	95
OPV3/DTaP-IPV-Hib	94.9
HepB3	91.5
Hib	94.1
At age 2	
MMR	84
DTP/DTaP-IPV-Hib rev. 1	88.7
OPV/DTaP-IPV-Hib rev. 1	83.8
At age 7	
DT rev. 2	92.8
OPV rev. 2	90.8
MMR rev. 1	87.5
At age 12	
HepB3	72.7
At age 14	
DT rev. 3	81.7
OPV rev. 3	67.6

Source: Institute of Public Health of Serbia 'Dr Milan Jovanovi Batut', 2016.

### Vaccination in Serbia

The beginnings of obligatory vaccination in Serbia date back to 1839. Following the European trends of that time, the first production of vaccines in Serbia started in 1900 in Nis [16].

For many years, the Torlak Institute of Virology, Vaccines and Sera has been manufacturing and distributing vaccines for compulsory immunization, prescribed by the Rulebook on Immunization and Manner of Protection with Medicines and the Calendar of Compulsory Vaccination in the Republic of Serbia.

Table 3 presents the results of the immunization carried out in the Republic of Serbia in 2015 [17]. It stems from the overview that the percentage of immunization by vaccines from the compulsory immunization programme was over 80%. The MMR vaccination at the age of two and the revaccination at the age of seven show less high coverage, with a scope of 84 and 87.5%. In the meantime, vaccines included in our compulsory immunization calendar in 2005—the vaccine against hepatitis B and in 2006—Hib vaccine, record first dose coverage of 91.5 and 95%.

The immunization calendar in Serbia has changed over the years. If we look back on the vaccines from the compulsory immunization defined by the Rulebook on Immunizations from 1991, on the list we will find the vaccines BCG, DTP, OPV, DT, dT, TT, the mono-vaccine against pertussis, and the vaccine against measles and mumps, whereas vaccination against rubella was compulsory only for female children [18]. In this sense, the immunization calendar in Serbia has changed and expanded to suit the needs of the population, in accordance with the new challenges of disease eradication by vaccination.

### Conclusion

Modern environment for the production and distribution of vaccines is characterized by globalization. In a dynamic environment, use of

strategic management by all players in the vaccine market—WHO, UNICEF, national institutions, manufacturers and distributors of vaccines—contributed to increasing immunization coverage worldwide.

Each country develops its own national immunization strategy, relying on WHO guidelines but respecting national characteristics—climate, local epidemiological, political and financial situation.

Further standardization and upgrading of GMP and GDP guidelines is expected.

Gradual cessation of administering vaccines against diseases which have been eradicated or are under control at the same time will be followed by the introduction of new vaccines and broadening of the immunization calendars. Therefore, in line with global changes, one may expect the enrichment of the immunization calendar in Serbia in terms of introducing the pneumococcal vaccine as compulsory for the entire population, as well as adding the HPV vaccine to the Serbian immunization calendar in the coming years.

In Europe, further expansion of administration of the herpes zoster vaccines expected, while further trend for the vaccine against hepatitis A is increasing the number of countries adding this vaccine to their programmes for certain groups of population. Global processes face the European Union with new challenges, that require new range of knowledge and new business strategy [19].

The vaccine market is growing rapidly and the accelerated technological development is being increasingly invested in, resulting in expensive vaccines.

The hypothesis that the application of strategic management approach increases both the effectiveness and the efficiency of organizations for vaccine production and distribution has been confirmed. The global goal of all parties is creating a world devoid of diseases that can be prevented by vaccination.

### Acknowledgements

We would like to thank Dr Peter Lachman for his valuable comments and suggestions on this research study.

### References

- Rabrenović M. Strategijski menadžment u javnom sektoru Beograd: JP 'Glasnik' & Eurosera; 2011.
- World Health Organization. *Topics*, 2016. [www.who.int/topics/vaccines/en](http://www.who.int/topics/vaccines/en) (25 January 2016, date last accessed).
- World Health Organization. *Biologicals*, 2016. [http://www.who.int/biologicals/vaccines/good\\_manufacturing\\_practice/en/](http://www.who.int/biologicals/vaccines/good_manufacturing_practice/en/) (25 January 2016, date last accessed).
- Council of the European Union. *Council Conclusions on Vaccinations as an Effective Tool in Public Health*. Brussels: Council of the European Union, 2014.
- World Health Organization. *Immunization*, 2015. [http://www.who.int/immunization/policy/Immunization\\_routine\\_table1.pdf?ua=1](http://www.who.int/immunization/policy/Immunization_routine_table1.pdf?ua=1) (November 2015, date last accessed).
- European Centre for Disease Prevention and Control. 2016. <http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx> (24 April 2016, date last accessed).
- WHO, Regional Office for Europe. *WHO, Regional Office for Europe (Vaccination Coverage)*, 2011–2013. <http://data.euro.who.int/cisid> (14 November 2017, date last accessed).
- WHO&UNICEF. *Global Immunization Vision and Strategy 2006–2015*, 2006. <http://www.who.int/immunization/givs> (18 October 2014, date last accessed).

9. Milstien JB, Kaddar M, Kieny MP. The impact of globalization on vaccine development and availability. *Health Aff (Millwood)* 2006;25: 1061–9.
10. U.S. Department of Health and Human Services, Centres for Disease Control and Prevention. 2016. <http://www.cdc.gov/vaccines/hcp/admin/storage/toolkit/storage-handling-toolkit.pdf> (1 July 2016, date last accessed).
11. Kaddar M. *Global Vaccine Market Features and Trends*. Geneva: WHO/IVB, 2012.
12. World Health Organization. *Immunization Standards*, 2015. [http://www.who.int/immunization\\_standards/vaccine\\_quality/en/](http://www.who.int/immunization_standards/vaccine_quality/en/) (20 November 2015, date last accessed).
13. World Health Organization. *Media Centre: Immunization Coverage*, 2016. <http://www.who.int/mediacentre/factsheets/fs378/en/> (21 July 2016, date last accessed).
14. Petrović R. *Imunizacije—Priručnik za primenu vakcina* Beograd: Velarta; 1996.
15. WHO & UNICEF. *Progress Towards Global Immunization Goals—2013, Summary Presentation of Key Indicators*. UNICEF&WHO, 2014.
16. Janković T. *Torlak 1930–1995* Beograd: 3M product, 1995.
17. Institute of Public Health of Serbia. 'Dr Milan Jovanović Batut'. Communicable diseases—results of conducted immunisation in Republic of Serbia, 2015. *Health Statistical Yearbook of Republic of Serbia 2015*, 2016 June: p. 418.
18. Petrović R. *Imunizacije—Priručnik za primenu vakcina* Beograd: Medicinska knjiga, 1993.
19. Radović-Marković M, Marković D, Radulović D. Critical competencies of virtual team members and its managers for business success. *International review* 2015;1–2:18.