

Poultry vaccines available on the Polish market after the harmonization of the pharmaceutical code according to EU legislation: an analysis of trends at the domestic versus global scale

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Summary

Poland's accession to the European Union (EU) has entailed the implementation of mutual recognition procedures for the authorization of immunological veterinary medicinal products (IVMPs) since 2009. The aim of the study was to analyse data on the assortment and number of doses in the batches of vaccines for poultry authorized on the Polish market in 2010. These data, compared with the total output of doses in the same batches of IVMPs manufactured worldwide, revealed trends in the application of poultry vaccines in Poland. The results of the survey indicate that poultry IVMPs were the most important immunologicals on the Polish market in terms of variety and the numbers of doses. The dominant position of poultry IVMPs against viral diseases on the Polish market reflected the global trend. They accounted for 97.98% of all poultry IVMPs, followed by anti-bacterial (1.55%) and anti-parasitic IVMPs (0.47%). The order of the five most popular poultry IVMPs was the same on the Polish market as in the global markets, namely vaccines against IB, IBD, ND, MD and TRT. In contrast, anti-bacterial vaccines against Salmonellosis (SE and ST) took the 8th place in terms of their share of the total number of doses manufactured and sold on the Polish market, whereas the total number of doses manufactured globally situated them at the 15th place. Moreover, the position of some anti-viral vaccines was substantially different in Poland; namely relatively high dose counts in vaccines against MD, TRT, DD and SHS, as opposed to rather low shares of vaccine doses against AE, AP, ILT from what these were on the global market. In conclusion, these differences require thorough analysis and the recognition of trends in supply and demand terms accordingly sustainable vaccination programming. The findings might reveal a gap between immunoprophylaxis guidelines and current immunoprophylaxis needs relevant to epidemiological status of poultry flocks in Poland.

Keywords: poultry vaccines, immunological veterinary medicinal products, veterinary pharmaceutical market, vaccine authorization

Legislation procedures for poultry vaccination at the national level after Poland's accession to the EU in 2004 have included the harmonization of the pharmaceutical code according to new rules since 2009. As a result, there has been a substantial change in trade conditions for the national market of immunological veterinary medicinal products (IVMPs, vaccines). Formerly, immunopreventive measures were based on

a limited range of IVMPs, originating from domestic biopharmaceutical plants and from other states of the Eastern Bloc. The development of mutual recognition procedures for authorization opened the domestic market to a variety of IVMPs offered by the worldwide biopharmaceutical industry. It has also created new possibilities for poultry vaccination outreaches at the national level (10).

Current authorization demands according to the mutual recognition procedure

There are three areas of action in the field of vaccine legislation: first, batch release and certification according to the Mutual Recognition Agreement between the EU member states; second, control testing of IVMP batches according to the European Directorate for the Quality of Medicines (3); and third, the quality testing of IVMP batches already released onto the market under a randomized surveillance program. These tasks in Poland are implemented according to the Official Control Authorized Batch Release (OCABR) or Official Batch Protocol Release (OBPR), which legitimizes the right of the marketing authorization holder (MAH) to distribute the product. The National Veterinary Research Institute (NVRI) in Puławy, carrying out official authorization procedures for immunological veterinary medicinal products, certifies the release of these products on the Polish market. Consequently, Poland as an EU member state started to proceed in agreement with the principle of mutual recognition, following the OBPR procedure according to Directives 2001/82/EC (European Parliament, 2001) and 2004/28EC (European Parliament, 2004). The data for the authorization of vaccine batches on the domestic market were collected for the first time in 2010. A database created during the authorization process has emerged as a potential source for the analysis of vaccination trends and their profiles for ruminants and swine at the national level (6, 7).

Rationale for the analyses of data on the authorization of vaccine batches at the national level

The main thesis of our research is the assumption that the quantity and assortment of vaccines offered by wholesalers on the open world market may serve as a reliable and representative standard of poultry vaccination. Further, we have assumed that the quantity of the doses within the particular vaccines released on domestic market, when confronted with the amounts of globally manufactured batches within the same IVMPs, may reflect relevant measures undertaken at the regional level in the immunoprophylaxis of poultry. Hence, to determine the compliance of trends in demand and supply terms of vaccines turnover on the Polish market with global poultry vaccination guidelines (1, 2, 9).

Alternatively, the profiles of regional vaccination programs may differ from the trends of poultry vaccination at a global-scale. In the first place, these differences may reflect a disparity in the epidemiological status of poultry flocks at the regional level and at the global level. On the other hand, the persuasive ability of wholesalers and/or specialists of poultry diseases recommending particular IVMPs may create an economic reality in demand and supply terms of poultry

vaccines turnover on the regional market. Hence, such a scenario implies an anticipation gap within immunological programs adopted in the control of poultry flocks' biosecurity (4, 5, 11).

The main aim of the study was a quantitative analysis of data from in-house records on the types and numbers of doses of poultry vaccines subjected to authorization procedures at the national level. The comparison of this in-house data with global figures on poultry vaccination made it possible to determine poultry immunoprophylaxis trends in Poland in the first period after the harmonization of the pharmaceutical code according to EU legislation. Conclusions and a discussion of issues related to high and recommendable standards of vaccination have been presented.

Statistical analyses of vaccine batch doses authorized on the Polish market in relation to their global output (P/G ratio)

According to Mutual Recognition Agreement procedures recorded in the NVRI data-base in 2010 comprised 711 (54.7%) applications for batches of the poultry vaccines, selected amongst a total of 1300 IVMPs batches for all animal species, and were authorized on the domestic market. Next, grouping of vaccine batches according immunoprophylaxis of specific poultry diseases, followed by assigning the number of doses within the vaccine batches (the dose pools) declared by the applicers for authorization on the national market were accounted. Subsequently, its confrontation with the total number of the produced doses within the same brands of the vaccine batches, their global worldwide output quoted by the manufacturers, served to compute national *versus* global proportion (P/G ratio). In addition, the domestic need for the vaccine dose numbers compared with entire doses of the same batches of brands being manufactured and offered worldwide, yielded IVMPs sequences accordingly to the viral, bacterial or parasitic prevalence of poultry diseases at both levels. At the same time, the reported system of result presentation was in compliance with recommendations of the European Medicines Agency, as it made it possible to omit the brand names of the vaccines (3). Hence, the confidentiality in respect to the scale of the vaccines trade offered on the market was achieved, because the information in the paper did not present the brand name of the IVMP, nor was the relation the of MAH with the particular product given. The dose pools of vaccine batches submitted for authorization were considered representative for the Polish market, because the system is based on mandatory regulations.

Outcomes of the analysis of vaccine batches authorized on the Polish market *versus* their output on the global scale

The analysis of the records indicated the domination of anti-viral vaccines, which accounted for 97.98%

Tab. 1. Sequence of the dose quantities of vaccine batches authorized in Poland *versus* total worldwide output of the doses and their ratio (P/G) within the same brands produced in 2010. Ranking was based on the amounts of doses assigned toward specific diseases aiming at poultry immunoprophylaxis

Immunoprophylaxis of poultry diseases		Ethiology of diseases	Species of poultry	Position at Polish market	Position at global output	National pool vs global output; P/G (%)
Infectious Bronchitis	IB	V	CH	1	1	8.1
Infectious Bursal Disease (Gumboro Disease)	IBD	V	CH	2	2	5.4
Newcastle Disease	ND	V	CH, T	3	3	7.9
Marek's Disease	MD	V	CH	4	4	20.7
Infectious Rhinotracheitis of Turkeys	TRT	V	T	5	5	17.5
Swollen Head Syndrome	SHS	V	CH	6	12	21.2
Avian reovirus infection	REO	V	CH	7	7	4.3
Salmonellosis (<i>S. Enteritidis</i> , <i>S. Typhimurium</i>)	SE-ST	B	CH	8	15	15.6
Egg Drop Syndrome	EDS	V	CH	9	8	5.2
Infectious laryngotracheitis	ILT	V	CH	10	6	2.8
Coccidiosis	KO*	P	CH	11	14	4.8
Fowl Typhoid (<i>S. gallinarum</i>)	SG	B	CH	12	13	4.0
Chicken Infectious Anemia	CAA	V	CH	13	11	2.4
Mycoplasmosis (<i>Mycoplasma gallisepticum</i>)	MG	B	CH	14	16	9.8
Avian pox	AP	V	CH	15	9	1.2
Avian Encephalomyelitis	AE	V	CH	16	10	1.2
Derzsy's disease	DD	V	G, MD	17	19	34.4
Ornithobacteriosis	ORT	B	CH, T	18	18	2.9
Colibacillosis	<i>E. coli</i>	B	CH	19	17	0.3
Average (\bar{x}):						$\bar{x} = 8.9$

Explanations: V – viral diseases; B – bacterial diseases; P – parasitic infection * own abbrev.; CH – chicken; T – turkey; G – goose; MD – mallard duck

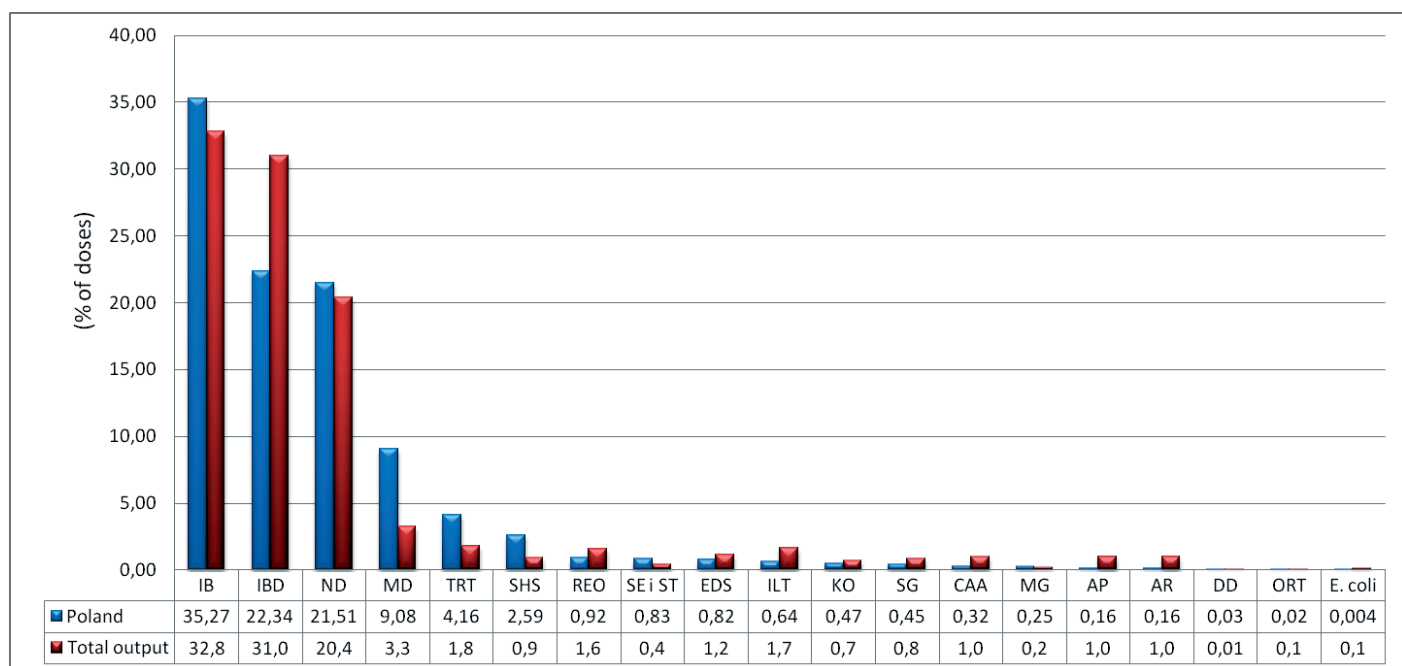


Fig. 1. Blue bars represent percentage share of doses devoted to particular poultry disease/syndrome among total doses of the poultry vaccine batches authorized on the Polish market. Red bars represent percentage share of the doses devoted to particular disease/syndrome among total output of the vaccine batches produced worldwide in 2010. Abbreviation names of the disease entities are found in Table 1.

of all IVMP doses authorized on the domestic market in 2010. Vaccines devoted to the prophylaxis of bacterial diseases accounted for 1.55%, followed by anti-parasitic IVMPs, 0.47%. The quantity of globally manufactured batches assigned to the mentioned groups of the pathogens scored 97.68%, 1.59% and 0.73%, respectively.

The ranking of the first five vaccines was the same for the domestic and global output (Tab. 1, Fig. 1). The highest number of doses was recorded for viral diseases, such as Infectious Bronchitis (IB), Infectious Bursal Disease (IBD) and Newcastle Disease (ND). For example, the batches of IB vaccines ranked in the first place numbered 6 771 488 500 globally produced doses, whereas a pool of 545 266 500 doses (ca 8% of total market) were authorized on the Polish market in 2010. Vaccines against IBD and ND – ranked second and third, respectively – shared a lower percentage of the overall market (Tab. 1). However, when compared with the above five IVMPs, a significantly higher P/G ratio within the vaccines against Marek's Disease (MD) and Infectious Rhinotracheitis of Turkeys (TRT) have been recorded. Even more significant differences were noted in the shares of IVMP batches for Swollen Head Syndrome (SHS) and Derzsy's Disease (DD). In the latter case, domestic vaccine doses accounted for 1/3 of the whole number of doses within the total batches. This finding demonstrated a relatively strong demand for the immunoprophylaxis of SHS and DD in Poland when compared to general trends. However, the trends in domestic demand for vaccines against Avian Reovirus Infection (REO), Egg Drop Syndrome (EDS), Infectious Laryngotracheitis (ILT), Chicken Infectious Anaemia (CAA), Avian Pox (AP) and Avian Encephalomyelitis (AE) were opposite to the above-mentioned, since they scored a lower P/G ratio.

Vaccines against bacterial diseases caused by germs of the *Enterobacteriaceae* family, *S. Enteritidis* (SE) and *S. Typhimurium* (ST) were at a relatively high, 8th place in the domestic ranking, whereas the global trend in demand and supply terms situated those IVMPs at the 15th place (Tab. 1). On the other hand, the IVMP dose pools for the immunoprophylaxis of other bacterial diseases, such as those caused by *S. gallinarum* (SG), *Mycoplasma gallisepticum* (MG) and *Ornithobacterium rhinotracheale* (ORT) did not differ in the Polish ranking from their positions within the global output of the same vaccine batches.

Vaccines against parasitic poultry diseases (coccidiosis) displayed similar ranking positions on Polish and international markets according to the respective number of doses within VMP batches (Tab. 1, Fig. 1).

Conclusions on vaccine trends in supply and demand terms and their relevance for poultry biosecurity

The profile of vaccinations against major poultry diseases displayed the same trend on both a domestic

and global scale. The ranking of the first five of the most frequently applied poultry IVMPs on the Polish market were exactly the same as the global profiles of the corresponding quantities of vaccine batches offered worldwide. This fact points to the proper adoption of vaccination measures to control the corresponding poultry diseases at the national level in 2010. At the same time, our hypothesis was supported by the finding that the quantity of vaccine doses needed for poultry, with respect to their analysis in demand and supply terms at the national versus global levels, is a representative and an appropriate instrument of adopted vaccination program according to their immunological status recognized within the local flocks.

On the other hand, the relatively high value of P/G ratios within the batches of MD, TRT, DD, SHS and, in contrast, its rather low value for AE, AP, ILT vaccines, may raise doubts about the correct adoption of vaccination guidelines at the national level in comparison with global trends of poultry immunoprophylaxis. It implies consideration of the alternative hypothesis of this paper, that high or low doses of quantity in IVMPs on the domestic *versus* global market reflected by P/G ratio may be not compliant with relevant vaccination needs at the regional scale. Obviously, the monitoring of serological status and/or identification of virus strains detected in the flocks at regional level is of primary importance, although it generates additional costs (2, 5, 10). The outcomes from the analysis of authorization data based on P/G ratio enabled the authors to demonstrate a potential anticipation gap at the national level for the above mentioned vaccines. Hence, the ranked values of the P/G ratio implying correctness of a sustainable vaccination program for the poultry justifies its adoption as an auxiliary source to serological diagnostic means.

The report on the failure of Avian Encephalomyelitis (AE) vaccination in Poland (11) may serve as an appropriate applicability of our ranking based on P/G ratio values. Namely, the 16th position of that disease at the national level compared to the 10th one within the whole IVMP output (Tab. 1) exemplifies relevance of Szeleszczuk's question about the ignorance or helplessness in case of AE immunoprophylaxis of domestic poultry (11). The result of data analysis from the authorization procedures, of this finding out the anticipation gap within the vaccines demand and supply terms, can serve as an additional instrument for the adoption of biosecurity programs based on immunoprophylaxis. That way, East's (2) study based on a questionnaire among breeders contributed to building up the sustainable vaccination guideline. It supports our finding on the relevance of data from authorization procedures for diagnosing or verifying immunoprophylaxis needs at the national or regional level.

In the case of bacterial diseases, the relatively high values of P/G ratio may reflect the specific immunological status of poultry salmonellosis in Poland. Global

trends show a rather low demand for IVMPs against bacterial diseases, which indicates the prevalence of antibiotic therapy against salmonellosis. At the same time, poor progress in the reasonable use of antibiotics in poultry can be concluded. However, complex salmonellosis eradication strategies in some countries additionally resulted in lower quantities of vaccines against salmonellosis used globally than in Poland.

Summing up, vaccination is considered as an important and prudent means of biosecurity measures undertaken both for industrial and free-range poultry farming (1, 8, 10). Furthermore, in case of the data shortage on the epidemiological status of poultry flocks deriving from serological diagnosis, motivation to adopt additional information sources was apparent (2). However, questionnaires among breeders' demands serving to plan the immunopreventive guidelines have been pointed out to be bound with some constraints (5, 10). The present results based on data from the mutual recognition procedure for IVMP authorization, which we used in our survey, proved their usefulness for an assessment of the vaccines demand and supply terms, as well as their relevance for immunoprophylaxis guidelines at the national level. Moreover, the outcomes are very representative due to authorization covering all vaccine batches released on the national market during a year. As a result, the standard of vaccination practice might be assessed with the use of the outcomes from official authorization procedures (OCABR), the applicability of which seems to be relevant for poultry experts and consultants.

Up until this juncture the data from vaccine authorization procedures have not been comprehensively applied, e.g. to assess an anticipation gap within the demand and supply terms at national level. According to the best of our knowledge, this paper presents the first attempt to relate the outcomes from such

an analysis with the adoption and/or verification of biosecurity guidelines by vaccination at the regional scale. As a reliable methodological tool it broadens the possibility for planning relevant immunoprevention procedures according to the current immunological status of the flocks.

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