



Adverse events following immunization during mass vaccination campaigns at first introduction of a meningococcal A conjugate vaccine in Burkina Faso, 2010

Claude-Roger Ouandaogo^a, Téné M. Yaméogo^e, Fabien V.K. Diomandé^{d,*}, Charles Sawadogo^a, Bassirou Ouédraogo^b, Rasmata Ouédraogo-Traoré^c, Lorenzo Pezzoli^f, Mamoudou H. Djingarey^d, Nehémie Mbakuliyemo^d, Patrick L.F. Zuber^g

^a Direction Générale de la Pharmacie, du Médicament et des Laboratoires (DGPML), Ministère de la santé, Ouagadougou, Burkina Faso

^b Direction de la Prévention par les Vaccinations (DPV), Ministère de la santé, Ouagadougou, Burkina Faso

^c Laboratoire de bactériologie et de Virologie, Centre Hospitalier Universitaire (CHU), Pédiatrie Charles-de-Gaulle, Ouagadougou, Burkina Faso

^d World Health Organization Inter-country Support Team for West Africa, Ouagadougou, Burkina Faso

^e Meningitis Vaccine Project (MVP), Bobo-Dioulasso, Burkina Faso

^f Consultant for the Meningitis Vaccine Project, London, UK

^g Immunization Vaccine and Biologicals, World Health Organization, Geneva, Switzerland

ARTICLE INFO

Article history:

Received 24 October 2011

Received in revised form

21 December 2011

Accepted 22 December 2011

Available online 9 January 2012

Keywords:

MenAfriVac

Safety

Pharmacovigilance

AEFI

Monitoring

Vaccine

Africa

ABSTRACT

*MenAfriVac*TM is a new meningococcal A conjugate vaccine developed to prevent meningitis outbreaks in Africa. It was first introduced during the last quarter of 2010 in three West African countries. We report on the monitoring of adverse events following immunization (AEFI) in Burkina Faso where more than 11 million people aged 1–29 years were vaccinated. Vaccine pharmacovigilance relied on stimulated passive AEFI surveillance countrywide and active surveillance for 12 clinical conditions in one sentinel district (Ziniaré) with 97,715 people eligible for vaccination. All AEFI occurring during the 10 days of mass campaign or the 42 subsequent days were to be notified. Serious AEFI were submitted to a national expert committee (NEC) for causality assessment. A total of 11,466,950 people were vaccinated with 1471 vaccinees reported to have experienced at least one AEFI (12.83 cases per 100,000). 1444 AEFI were minor; the most common of which were fever, headache, gastro-intestinal disorders and local reactions (2–7 cases per 100,000). Of 27 serious AEFI reported, four cases were classified by the NEC as related to vaccine (1 case per 3 million vaccinated) including one case each of exanthematous pustulosis, angioedema, bronchospasm and severe vomiting. Active surveillance identified 71 cases of the 12 conditions of interest. Convulsions, urticaria and bronchospasm were more frequently reported. Attack rates for those conditions were similar to the baseline rates recorded in the same population, over the same time period, a year earlier. With the exception of convulsions in the days following vaccination the distribution of time intervals between vaccination and the occurrence of symptoms did not reveal any temporal clustering. The monitoring of AEFI of *MenAfriVac*TM in Burkina Faso did not suggest special concern regarding the vaccine safety. However, reported possible hypersensitivity reactions to vaccine components would require further review to rule out any anaphylactic reaction.

Published by Elsevier Ltd.

1. Introduction

Epidemic meningitis is a significant cause of morbidity and mortality in sub-Saharan Africa, in an area stretching from Senegal to Ethiopia, designated as the meningitis belt. In this area, epi-

demic meningitis is primarily caused by serogroup A meningococci (NmA), with disease incidence peaking in the dry season every year.

*MenAfriVac*TM is a new meningococcal serogroup A conjugate vaccine developed by the Meningitis Vaccine Project (MVP) [1] and Serum Institute of India (SII) Ltd. It was licensed in India in January 2010 and was prequalified by the World Health Organization (WHO) in June 2010 [1,2]. Clinical trials conducted among people aged 1–29 years old in India and Africa have demonstrated that *MenAfriVac*TM has a safety profile similar to that of a licensed polysaccharide vaccine but elicits a significantly stronger and more persistent immunological response against group A meningococcus and has the ability to induce immunologic memory [3]. In order to

* Corresponding author at: Meningitis Vaccine Project, Immunization and Vaccine Development, World Health Organization Inter-country Support Team for West Africa, 03 BP 7019 Avenue de l'Indépendance, Ouagadougou, Burkina Faso.

Tel.: +226 75 44 22 90; fax: +226 50 33 25 41.

E-mail addresses: fabien.diomande68@gmail.com, diomandef@bf.afro.who.int (F.V.K. Diomandé).

systematically collect additional safety data careful post-marketing surveillance [4,5], WHO Global Advisory Committee on Vaccine Safety (GACVS) [4], recommended a phased introduction of the vaccine in countries of the meningitis belt through mass vaccination campaigns targeting individuals aged between 1 and 29 years of age (eligible individuals).

Burkina Faso, Mali and Niger, all in West Africa, were the first countries to introduce the vaccine. The first phase (Phase A) of introduction was conducted in September 2010 and involved approximately 400,000 eligible individuals per country living in one or two districts. The second phase (Phase B) occurred in December 2010 in the three countries and involved a total of 18 million eligible individuals.

In Burkina Faso, the health district of Kaya with 350,145 eligible individuals and located in the Central-North part of the country 100 km from the capital city Ouagadougou, was chosen for Phase A. While Phase B covered the 62 remaining health districts and 10,783,686 eligible individuals.

The systematic surveillance of the adverse events following immunization (AEFI) forms part of the development plan for any medicinal product or vaccine, even after licensure. The rapid introduction of *MenAfriVac*TM among large populations required consideration of the potential occurrence of infrequent serious AEFI that could have been missed during the clinical trials involving smaller numbers of subjects. In order to address this, the monitoring of AEFI was conducted during and after mass immunization campaigns, based on existing national vaccine adverse events monitoring systems. This paper describes methods and results of *MenAfriVac*TM AEFI surveillance during Phases A and B of vaccine introduction in Burkina Faso.

2. Methods

2.1. Definition of adverse events following immunization

An AEFI was defined as any health event, occurring within 42 days in subjects that were vaccinated during the *MenAfriVac*TM vaccination campaigns in Burkina Faso (Phases A and B). Cases were defined as serious, if they involved hospitalization, were life-threatening conditions, onset of disability or death, or minor if they did not fall into this category.

2.2. Stimulated passive surveillance of AEFI

The Burkina Faso Ministry of Health implemented an enhanced spontaneous AEFI surveillance system, during Phases A and B, from the first day until 42 days after the campaign. Surveillance tools, namely a field guide including case definitions and standard operation procedures, a case-based notification form, and an investigation form for serious cases were developed and made available (in French). The existing national pharmacovigilance system was enhanced through training, dissemination of updated AEFI monitoring guidelines and reminders about AEFI reporting during supervisory visits at all levels of the health care system. Country coordination, clinical management teams and a laboratory focal point, as well as a National Experts Committee (NEC) were designated. At district health level, population was sensitized and healthcare workers trained. This surveillance system aimed at detecting, reporting, investigating, classifying AEFI cases and allowing their proper clinical management. All cases were to be notified using the notification form. In addition, serious cases were to be reported with their investigation form within 24 h to AEFI coordination teams at district, region and national levels. All forms were sent to the national coordination team for processing.

2.3. Causality assessment and classification of serious AEFI

Only serious cases were submitted to the NEC for causality assessment. The committee requested further clinical and/or laboratory investigations as needed. For each serious case a final classification was provided according to the following categories: vaccine-related (which has a further classification in possibly vaccine-related or probably vaccine-related), co-incidental, program error, non classifiable or indeterminate.

2.4. Active adverse events sentinel surveillance

Active AEFI surveillance was implemented in the district of Ziniaré, during Phase B (10 days of vaccination campaign and 42 days following the campaign) to systematically monitor selected events that could possibly be related to vaccination, as recommended by the GACVS. Sixteen health posts, among 45 in the whole district, serving 97,715 vaccine eligible people, were selected as sentinel sites for active surveillance. The focus was on 12 clinical conditions (local abscess, urticaria, anaphylactic shock, bronchospasm, laryngeal edema, toxidermia, purpura, convulsions, meningitis syndrome, hypotonia, flaccid paralysis, encephalomyelitis) for which case definitions were developed. Specific reporting forms were designed and the health posts were visited weekly by designated supervisors. During the 10 days of the campaign and 42 days thereafter, all cases of the 12 clinical conditions in vaccines who reported to one of the 16 health centers were recorded after verification of their vaccination status.

2.5. Retrospective review of selected outcomes of interest

In order to compare AEFI reports with the pattern of morbidity usually seen in the population, we assessed background occurrence of health events by reviewing the frequency of those events in the same population in the absence of vaccination. Patients care registries from the same 16 health care facilities were reviewed to enumerate the occurrence of the 12 selected outcomes of interest for the corresponding time period of 2009 in the same age group.

2.6. Data analysis

We described frequencies of health problems reported, analyzed their occurrence according to vaccination period, estimated rates of AEFI, and compared estimates with baseline data. Regarding active surveillance data, estimated AEFI rates were extrapolated from a sample toward the parent population, and confident intervals of 95% were constructed.

3. Results

3.1. Enhanced passive surveillance for adverse events

During Phase A, in the district of Kaya from 20th to 29th September 2010, 349,395 individuals were vaccinated with *MenAfriVac*TM. During Phase B, that included the rest of the country from 6th to 15th December 2010, 11,117,555 people were vaccinated, making a total of 11,466,950 eligible individuals (1–29 years). The age distribution of vaccinated persons was: 1–4 years 20.96%, 5–14 years 40.99%, and 15–29 years 38.05%.

A total of 1471 patients experienced at least one AEFI: 1444 were classified as minor cases at health facility level and 27 considered as serious cases after field investigations (Fig. 1). The overall attack rate was 12.83 AEFI cases per 100,000 people vaccinated, ranging from 1.41 in the region of “Plateau central” to 26.03 per 100,000 in the region of the “Boucle du Mouhoun”. Because a patient could present more than one AEFI, a total of 2008 minor

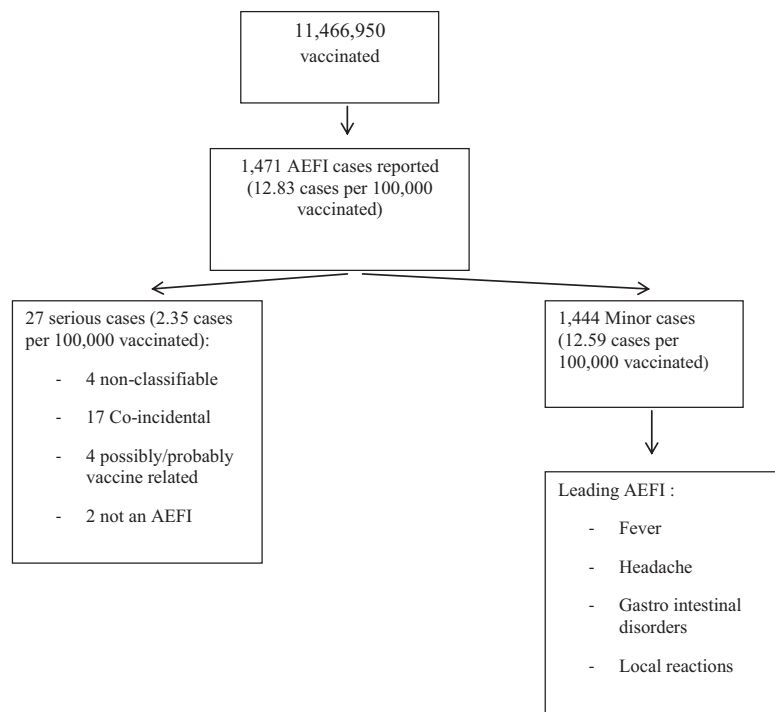


Fig. 1. Reporting and classification of AEFI cases through enhanced passive AEFI surveillance.

Table 1

Attack rates of minors AEFI recorded ($N = 11,466,950$ persons vaccinated).

AEFI	<i>n</i>	Attack rate ^a
Fever	779	6.79
Headache	310	2.70
Gastro intestinal disorders	265	2.31
Local reactions	227	1.98
Dizziness/syncope	120	1.05
Myalgia	96	0.84
Urticaria/pruritis/rash	84	0.73
Persisting crying	29	0.25
Arthralgia	24	0.21
Convulsions	17	0.15
Abscess	16	0.14
Sleeping disorders	14	0.12
Asthenia/lethargy	15	0.13
Eczema	6	0.05
Lymphadenopathy	5	0.04
Persisting nodules	1	0.01
Total	2008	17.51

^a Number of cases per 100,000 persons vaccinated.

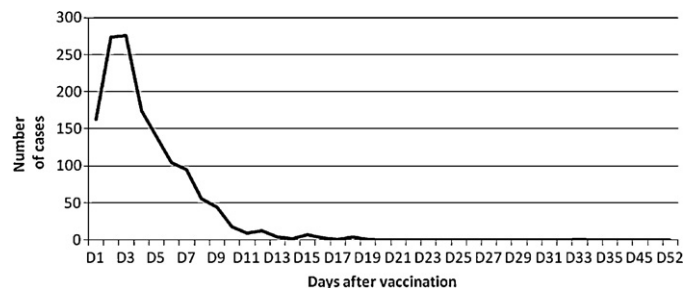


Fig. 2. Onset of AEFI cases reported through enhanced countrywide passive surveillance.

events were recorded. Fever, headache, gastro-intestinal disorders and local reactions were the four most frequently AEFI reported (Table 1). Fever and gastro-intestinal disorders were most frequent among younger subjects (1–14 years old) while headache and local reactions were observed more frequently in the older age group (15–29 years old) (Table 2). Also, gastro-intestinal disorders

were more frequently observed among females (155 of 264 events, 58.71%) compared to males (41.29%), while local reactions were more frequently reported by males (122 of 225 events, 54.22%) compared to females (45.78%) while the others were equally distributed. Only 17 cases of convulsions were reported and among them, 12 occurred within 4 days after vaccination. All AEFI were reported during the first 16 days of surveillance and 96.70% of them were reported during the 10 days of the mass campaign period (Fig. 2). Except for local reactions, the attack rates of the most frequent AEFI were much lower than the background occurrence of similar health problems and regardless of the age group (Table 2).

Of 27 reported serious AEFI which were reviewed by the NEC, 4 cases were “unclassifiable” (not enough reliable information to

Table 2

Attack rates of most frequent AEFI reported compared to baseline data and by age group.

AEFI	AEFI attack rate ^a /baseline rate			
	1–4 yo (<i>n</i> = 2,403,662)	5–14 yo (<i>n</i> = 4,699,895)	15–29 yo (<i>n</i> = 4,363,393)	Total (<i>N</i> = 11,466,950)
Fever	14.10/5,062.90	5.51/709.42	3.99/509.29	6.79/1,636.18
Headache	0.83/31.23	2.60/59.95	3.76/115.86	2.70/72.54
Gastro intestinal disorders	5.08/301.05	1.94/25.98	1.10/53.35	2.31/53.35
Local reactions	1.00/0	1.87/0	2.59/0	1.98/0

^a Number of cases per 100,000 persons vaccinated.

Table 3
Reported AEFI cases through active search in the district of Ziniaré.

12 syndromes	Rates of health problems ^a					
	Active search-2010 (N = 107,493 vaccinated)			Baseline data-2009 (N = 97,715 surveyed)		
	n	Rate	95% CI	n	Rate	95% CI
Convulsions	32	29.76	19.44–40.07	26	26.60	16.37–36.82
Urticaria	18	16.74	9.00–24.47	21	21.49	12.29–30.68
Bronchospasm	14	13.02	6.19–19.84	16	16.37	8.34–24.39
Meningitis syndrome	3	2.79	–0.36 to +5.94	3	3.07	–0.40 to +6.54
Local abscess	1	0.93	–0.89 to +2.75	0	0.0	0
Hypotonia	2	1.86	–0.71 to +4.43	0	0.0	0
Toxidermia	0	0.0	0	1	1.02	–0.98 to +3.02
Flaccid paralysis	0	0.0	0	1	1.02	–0.98 to +3.02
Laryngeal edema	1	0.93	–0.89 to +2.75	0	0.0	0
Encephalomyelitis	0	0.0	0	0	0.0	0
Purpura	0	0.0	0	0	0.0	0
Anaphylactic shock	0	0.0	0	0	0.0	0
Total	71	66.05	50.68–81.41	68	69.59	53.04–86.13

^a Number of cases per 100,000 persons vaccinated.

be classified), 17 cases were “co-incidental”, 2 cases did not meet the case definition and 4 cases were possibly (2 cases) or probably (2 cases) related to vaccine administration (Fig. 1). The four probably/possible vaccine-related cases, were of exanthematous pustulosis, angioedema, bronchospasm and serious vomiting. They were treated according to the existing clinical standard of care and all recovered.

3.2. Active sentinel surveillance for adverse events

In parts of Ziniaré, active surveillance identified 71 cases of the 12 conditions of interest. Of the 12 selected conditions under active surveillance, 3 were more frequently reported with attack rates, respectively, of 29.76 per 100,000 persons for convulsions, 16.74 for urticaria and 13.02 for bronchospasm (Table 3). The number of cases at each time interval post-vaccination was similar for urticaria and for bronchospasm. There was a slightly higher number of convulsions (8 cases) within the first 4 days after vaccination (Fig. 3) as compared to all other time intervals (0–4 cases). AEFI distribution and attack rates were similar to the baseline rates recorded for similar health problems in the same facilities 1 year before the mass campaign (Table 3). Of note, the distribution of time intervals between vaccination and the occurrence of the three conditions with more than 10 cases identified did not reveal any temporal clustering. Five of the 12 selected conditions have not been detected through active search in this population during the active surveillance period: anaphylactic shock, toxidermia, purpura, flaccid paralysis and encephalomyelitis (Table 3).

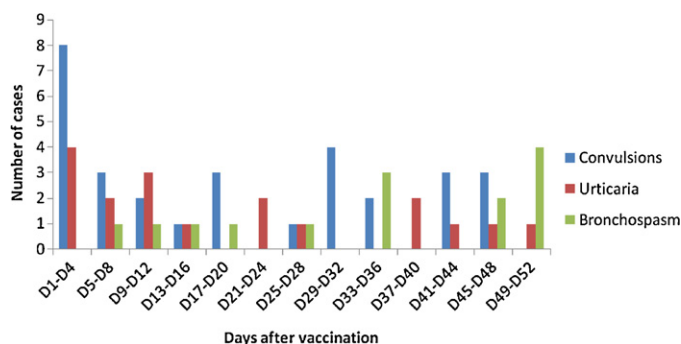


Fig. 3. Onset of main selected conditions reported through active search in the district of Ziniaré.

4. Discussion

*MenAfriVac*TM was introduced in Burkina Faso over a 4-month period (September–December 2010) through two mass vaccination campaigns. During the vaccination campaigns and up to 6 weeks after, enhanced passive and sentinel active surveillance systems were set up for the AEFI monitoring. More than 11.4 million doses were administered and 1471 patients experienced at least one AEFI. Only four of the 27 serious AEFI cases notified were considered as vaccine-related, these were: one case of exanthematous pustulosis, one angioedema, one bronchospasm and one case of serious vomiting. The active surveillance exercise conducted in parts of one sentinel district showed a preponderance of non-delayed and common AEFIs.

The most common minor AEFIs reported: fever, headache, gastrointestinal disturbances and local reactions at the injection site were acute events, usually within 5 days after vaccination. These events, were also reported during clinical trials of *MenAfriVac*TM [3], and are common to most vaccines. Local reactions, nausea, vomiting and fever to a lesser extent were frequently associated with meningitis C conjugate vaccine [9]. With pneumococcal conjugate vaccine, local reaction and fever were the most reported AEFI in children less than 5 years [10]. Local reactions at the injection site were more frequent with *MenAfriVac*TM than polysaccharide ACWY vaccine during clinical trials [3]. Vaccine conjugation with tetanus toxoid, the carrier protein for the *MenAfriVac*TM is known to lead to the risk of local reaction at the injection site and sterile abscess [11]. This risk should increase in case of contact between adjuvant (aluminum hydroxide) and subcutaneous tissue during the injection [11]. Therefore, abscesses at the injection site reported during surveillance may be due to a vaccine reaction (sterile abscess) or may be related to program errors (improper aseptic methods). The surveillance system in place does not allow distinguishing between these two causes. However, an attack rate of 0.14 cases of local reactions per 100,000 vaccinated is much lower than rates usually reported of 6–10 cases of sterile abscesses per 1 million tetanus toxoid doses administered [12]. This could indicate good vaccine injection practices during the campaign, a lower vaccine reactogenicity compared with the tetanus vaccine or a limited sensitivity of the surveillance system. Implementation of safe injection policies and practices in the Expanded Program of Immunization (EPI) and many Supplemental Immunization Activities (SIA) during the past 2 decades may also have contributed to the overall reduction in the rate of program errors [13,14].

Fever and gastrointestinal disorders were mainly observed in children between 1 and 4 years of age. Although fever is a common

response following immunization [15,16], other common causes of fever in the local settings should also be taken into account in the interpretation of this information. Burkina Faso experiences a high incidence of infectious diseases with the preponderance of malaria, pneumonia and diarrheal diseases in the age group of 0–5 years [17], all of which are common causes of fever. Some cases of these diseases could have been coincided with vaccination. The epidemiology of these common causes of fever could also explain the higher rates of AEFI in some areas compared to others. Except for local reactions at the injection site, rates of reported AEFI were dramatically lower than background rates of similar health problems occurring during the same period. This most likely reflects under-reporting of AEFI which is typical to such a passive surveillance.

Among more than 11 million people vaccinated in Burkina Faso, very few serious AEFI were reported (27 cases). Most of these cases were classified by the NEC as coincidental or not classifiable due to insufficient data. Only four cases were classified as possibly or probably related to the vaccine (approximately 1 case per 3 million vaccinated). Three of the four vaccine-related severe cases were bronchospasm, angioedema and acute generalized exanthematous pustulosis. This could suggest hypersensitivity to the vaccine components as is the case with many other vaccines [18,19] but would require additional assessment. Significantly there is no death reported as linked to the vaccine.

The profile of reported AEFI cases during active surveillance in Ziniaré showed a preponderance of non-delayed and common AEFI. Those included hypersensitivity reactions (urticaria, bronchospasm) and convulsions, mostly classified by the NEC as coincidental reactions as they were more common in children and found to be linked to malaria and other common diseases in that area. Also, the under reporting rate of convulsions during passive surveillance phase is typical of such a self-reporting surveillance system, as described above. Indeed, convulsions are frequently associated with most of the background diseases in this area. Therefore, they are not spontaneously reported as AEFI at health posts. However, special attention should be given to monitoring of non-delayed symptoms, including convulsions, during future campaigns. Rare or delayed AEFI such as Guillain–Barré syndrome or encephalomyelitis were not detected, however it is unlikely that these would have occurred in such a small population (107,493 vaccinated).

4.1. Limitations

Passive AEFI surveillance, although strengthened during the introduction of *MenAfriVac*TM, is subject to the traditional limitations of such a system. These include inadequate training of health care workers in basic AEFI surveillance, under-reporting of cases, inadequate application of standard case definitions, lower quality and completeness of data reported, and the variability in the reporting of cases depending on areas and profiles of notifiers [6,7]. Indeed, we noted that while 52.10 cases (of only 7 conditions) per 100,000 vaccinated were notified through active search, the overall notification rate for passive surveillance was only 12.83 cases per 100,000 vaccinated with an interregional variability ranging from 1.41 to 26.03 cases per 100,000 vaccinated. However, this notification rate was far higher than the rates reported in previous mass vaccination campaigns in Burkina Faso. In 2003, during mass vaccination campaign with trivalent meningococcal polysaccharide ACW135 vaccine, AEFI reporting rate was 5.9 cases for 100,000 doses administrated [8]; in 2008, it was 3.6 during the mass campaign with yellow fever vaccine which targeted 7 million people (unpublished Ministry of Health reports). This may attest to the strengthening of local pharmacovigilance system whose formal structure, currently being formalized, was first tested in the AEFI surveillance effort presented here. Minor AEFI cases reported

were not investigated, in accordance with the surveillance procedures. Their relationship to the vaccine was considered as temporal and do not necessarily reflect a causal association with the vaccine. Therefore, calculated attack rates for passive surveillance should be considered as minimum attack rates.

The observed higher reliability of the active surveillance data despite the fact that it took place in a smaller cohort, raises an interest and focus on active AEFI search as a reliable approach to assessing vaccine safety in post introduction period in developing countries. However, and as we have seen, the implementation of active AEFI surveillance requires more logistics, resources and person-times. Also, its implementation at a shorter scale does not allow detecting rare or delayed AEFI. Therefore, these two approaches should complement each other, and depending on relevant evaluation questions and resources available.

5. Conclusions

This experience with AEFI monitoring through countrywide enhanced passive and sentinel active surveillance did not identify outstanding safety issues with *MenAfriVac*TM. The actual safety profile documented is consistent with that of other monovalent polysaccharide conjugate vaccines such as those against *Haemophilus influenzae* type b. However, reported possible hypersensitivity reactions to vaccine components requires further attention through the countries yet to rollout this vaccines in order to rule out any association of vaccine components with anaphylactic reactions. Ensuring proper pharmacovigilance was challenged with the limited development of national AEFI monitoring systems in the three countries. This report from Burkina Faso provides important insights for preparing other introductions of new vaccines specifically designed for resource-poor countries.

Conflict of interest statement

None declared.

Acknowledgments

We thank the residents in all the districts of Burkina Faso for their participation in the surveillance of AEFI, the health care workers from districts and regions involved. We thank the members of the National Experts Committee (NEC), the Direction Générale de la Pharmacie du Médicament et des Laboratoires (DGPML), the Direction de la Prévention par la Vaccination (DPV), the Direction de la Lutte contre la Maladie (DLM), the WHO country office in Ouagadougou, the Immunization and Vaccine Development (IVD) team at WHO Intercountry Support Team for west Africa in Ouagadougou, WHO regional office for Africa (AFRO) in Brazzaville, and WHO Headquarter in Geneva for their contributions. Special thanks for the members of the Global Advisory Committee on Vaccine Safety (GACVS) who closely monitored the planning and implementation of AEFI surveillance of *MenAfriVac*TM and who reviewed the data collected. We would like to thank Dr. Rigobert Thiombiano (Infectious disease unit at University teaching hospital of Yalgado-Ouédraogo in Ouagadougou), Dr. Mahamadou Compaoré (Former Director of DGPML), Dr. Jean-Batiste Nikiéma (Director of DGPML), Dr. Arsène Ouédraogo (DGPML), Dr. Fenella Avokey (Focal point IVD sub-cluster at WHO IST WA), Dr. Touré Bokar (Coordinator WHO IST WA), Dr. Djamilia Cabral (WHO representative in Burkina Faso), Dr. Carol Tevi-Benissan (MVP focal point at WHO Headquarter Geneva), Dr. Mihigo Richard (Focal point for new vaccine introduction at WHO AFRO), Dr. William Perea (WHO Headquarter Geneva), Dr. Marie-Pierre Preziosi (WHO Headquarter Geneva) and Dr. Marc LaForce (Director of MVP) for their

support to *MenAfriVac*TM pharmacovigilance. Special acknowledgements are given to Mr. Lingani Clement for his role in the data management and to Professor Bartholomew Dicky Akanmori from the IVD cluster at WHO AFRO who accepted to review this paper.

References

- [1] LaForce FM, Konde K, Viviani S, Préziosi MP. The Meningitis Vaccine Project. *Vaccine* 2007;25(Supplement 1):A97–100. Epub 2007 May 7.
- [2] Bishai DM, Champion C, Steele ME, Thompson L. Product development partnerships hit their stride: lessons from developing a meningitis vaccine for Africa. *Health Aff (Millwood)* 2011;30(June (6)):1058–64.
- [3] Sow SO, Okoko BJ, Diallo A, Viviani S, Borrow R, Carlone G, et al. Immunogenicity and safety of a meningococcal A conjugate vaccine in Africans. *New Engl J Med* 2011;364(June (24)):2293–304.
- [4] Global Advisory Committee on Vaccine Safety, 3–4 December 2009. *WER* 2010;85(5):31–2.
- [5] Global Advisory Committee on Vaccine Safety, 16–17 June 2010. *WER* 2010;85(30):285–92.
- [6] Vogt RL, LaRue D, Klaucke DN, Jillson DA. Comparison of an active and passive surveillance system of primary care providers for hepatitis, measles, rubella, and salmonellosis in Vermont. *Am J Public Health* 1983;73(July (7)):795–7.
- [7] Ciofi Degli Atti ML, Salmaso S, Bella A, Arigliani R, Gangemi M, Chiamenti G, et al. Pediatric sentinel surveillance of vaccine-preventable diseases in Italy. *Pediatr Infect Dis J* 2002;21(August (8)):763–8.
- [8] Bentsi-Enchill AD, Zongo I, Khamassi S, Pless R, Thombiano R, Tiéndrebéogo S, et al. Monitoring of adverse events during the 2003 mass vaccination campaign with a trivalent meningococcal A/C/W135 polysaccharide vaccine in Burkina Faso. *Vaccine* 2007;25(Supplement 1):A72–8. Epub 2007 May 7.
- [9] Pöllabauer EM, Petermann R, Ehrlich HJ. Group C meningococcal polysaccharide-tetanus toxoid conjugate vaccine: a meta-analysis of immunogenicity, safety and posology. *Hum Vaccin* 2005;1(July–August (4)):131–9. Epub 2005 July 13.
- [10] Destefano F, Pfeifer D, Nohynek H. Safety profile of pneumococcal conjugate vaccines: systematic review of pre- and post-licensure data. *Bull World Health Organ* 2008;86(May (5)):373–80.
- [11] Mark A, Carlsson RM, Granstrom M. Subcutaneous versus intramuscular injection for booster DT vaccination of adolescents. *Vaccine* 1999;17(April (15–16)):2067–72.
- [12] WHO. Supplementary information on vaccine safety. Part 2: background rates of adverse events following immunization. WHO/V&B/00.36; 2000. Available on: <http://www.who.int/immunization.safety/publications/aefi/en/>.
- [13] Kane M. Unsafe injections. *Bull World Health Organ* 1998;76(1):99–100.
- [14] Cutts FT. Advances and challenges for the expanded programme on immunization. *Br Med Bull* 1998;54(2):445–61.
- [15] Kohl KS, Marcy SM, Blum M, Connell JM, Dagan R, Hansen J, et al. Fever after immunization: current concepts and improved future scientific understanding. *Clin Infect Dis* 2004;39(3):389–94.
- [16] Michael MS, Kohl KS, Dagan R, Nalin D, Blum M, Jones MC, et al. Fever as an adverse event following immunization: case definition and guidelines of data collection, analysis, and presentation. *Vaccine* 2004;22(5–6):551–6.
- [17] Müller O, Traoré C, Becher H, Kouyaté B. Malaria morbidity, treatment-seeking behaviour, and mortality in a cohort of young children in rural Burkina Faso. *Trop Med Int Health* 2003;8(April (4)):290–6.
- [18] Laribié A, Miremont-Salamé G, Reyre H, Abouelfath A, Liège L, Moore N, et al. Surveillance of adverse effects during a vaccination campaign against meningitis C. *Eur J Clin Pharmacol* 2005;61(December (12)):907–11. Epub 2005 November 18.
- [19] Vellozzi C, Broder KR, Haber P, Guh A, Nguyen M, Cano M, et al. Adverse events following influenza A (H1N1) 2009 monovalent vaccines reported to the Vaccine Adverse Event Reporting System, United States, October 1, 2009–January 31, 2010. *Vaccine* 2010;28(October 45):7248–55. Epub 2010 September 16.