

# HOW TO REACT QUICKLY IN FRONT OF EPIDEMIOLOGICAL ALERTS: APPLICATION TO ZIKA ALERT BY THE FRENCH ADVISORY GROUP

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## BACKGROUND

The French advisory group (FAG) for safety of Substances of Human Origin is dedicated to issuing recommendation about measures to be implemented in case of epidemiological alerts, in order to prevent transfusion-transmitted infections for pathogens not usually screened in blood donors. The scope was initially focused on Arboviruses (Dengue, Chikungunya, WNV and recently Zika) but was, over the years, expanded to other pathogens: plasmodium, Coronavirus and Ebola. The role and the missions of the advisory group are described in a guideline to avoid introduction of Chikungunya, Dengue and West Nile Virus (WNV) in metropolitan France. This guideline is implemented under the aegis of the Ministry of Health (DGS).

## PURPOSE

The advisory group is steered by the French National Agency for Medicine and Health Products Safety (ANSM) and gathers experts and representatives of national institutions: Biomedicine Agency (ABM), National Reference Laboratories for each pathogen (CNR), Regional Haemovigilance Coordinators (RHC), Military Blood Centre (CTSA), Ministry of Health (DGS), National Blood Service (EFS) and French Institute for Public Health Surveillance (InVS). Epidemiological alerts are forwarded to ANSM by InVS. Depending on alert severity, ANSM triggers a face to face meeting (or a teleconference in case of emergency) of the advisory group in order to discuss possible measures taking into account available epidemiological data, pre-existing decisions and impact on blood components availability. Measures withdrawal, at the end of the epidemics, is also discussed.

## METHODS

Concerning Dengue, Chikungunya or WNV alerts, the advisory group is activated as soon as pre-established specific criteria are met for French metropolitan department, overseas department (Antilles and Réunion) and foreign countries, depending on previous viral circulation in these different areas (Table 1). For each alert, possible measures applying to donor selection (temporary deferrals), donation screening (supplementary testing), blood components processing (quarantine, pathogen reduction technologies) or issuing (specific indication by patient category of inactivated, extra screened or collected outside of the alert area blood components) are discussed. Strategies are annually reviewed and updated.

**Table 1: Alert threshold to activate advisory group per area and pathogen**

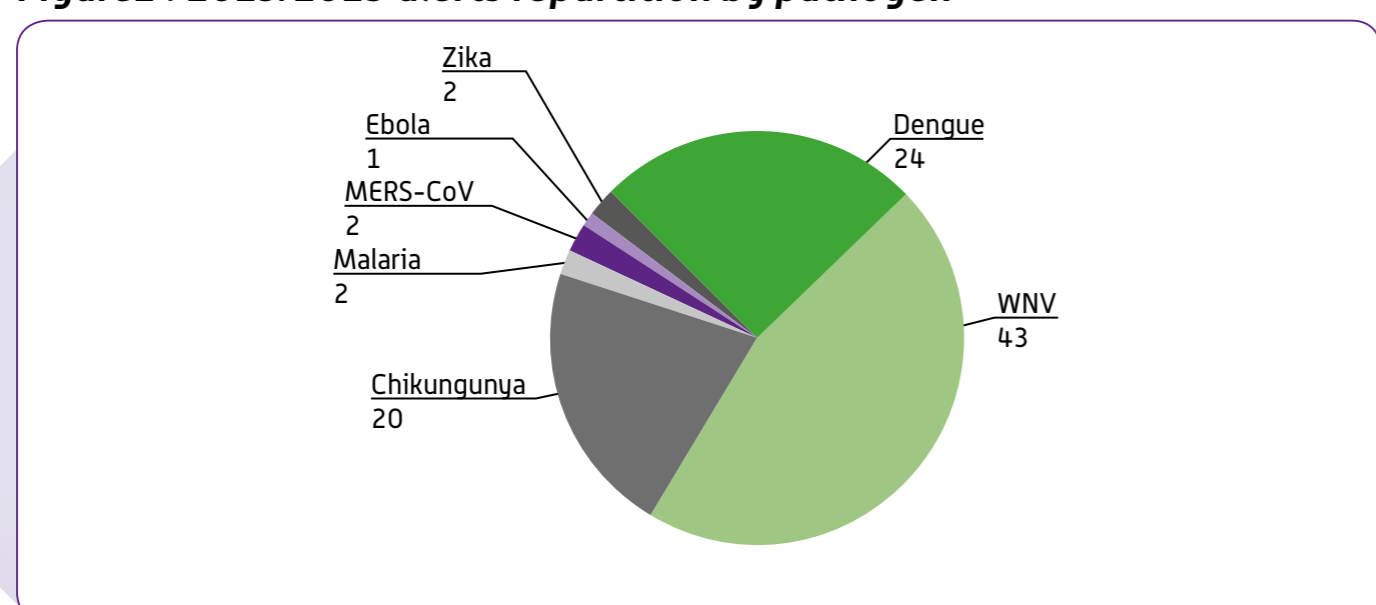
Area / Pathogen	Metropole / Réunion	Antilles	Foreign countries
Dengue + Chikungunya	Cluster of autochthonous cases	Confirmed epidemic	Epidemic + area not concerned by Malaria or Chagas + imported cases from this area in France
WNV	1 autochthonous case	1 autochthonous case	Depending on country and epidemiological situation when not listed at beginning of the season

## RESULTS

In 2013/2015, the advisory group managed 163 alerts convened 54 times and recommended 38 preventive measures and 9 measures withdrawal (figure 1). Some measures were implemented:

- in advance (WNV at the starting of season according to previous season cases): adequacy between that donor deferral strategy planned in advance and the real cases finally reported by each country is shown in table 2;
- according to an existing guideline (Dengue, Chikungunya, WNV) when alert is reported;
- following (re-)emergence of pathogens. Example is given focusing on Zika virus epidemic alerts that occurred in 2015 or are still ongoing today.

**Figure 1 : 2013/2015 alerts repartition by pathogen**



For Zika alerts, viral circulations were reported since November 2013 in Pacific islands, Brazil and Columbia but pre-existing measures were already applied against Dengue, Malaria or Chagas. These measures cover blood donors coming back from Zika alert areas (temporary deferral period greater or equal to 28 days).

Alert level changed when new territories in America and new identified risks emerged (microcephaly and Guillain-Barré syndromes) even if still not definitely and totally imputed to Zika virus.

Measure (temporary deferral of 28 days after return) was recommended in November 2015 when first territory (Cape-Verde) without pre-existing measure reported autochthonous Zika virus cases.

When first autochthonous cases appeared in French Guiana and Martinique in mid-December 2015, some measures were already implemented against Dengue. FAG was activated, following the alert threshold established during 2013-2014 Chikungunya epidemics in French Caribbean departments, to assess the efficiency of these measures against Zika virus infection:

- Temporary deferral (28 days) of donors who stayed at least one night in the affected areas during the last 28 days.
- Reinforcing physician (health professional) information about search of evocating symptoms. Temporary deferral in case of symptoms (14 days for fever).
- Reinforcing donor information about post-donation information.
- 72 hours quarantine for Red Blood Cell Concentrates.
- Pathogen reduction treatment of all Platelet Concentrates.
- Plasma supply from French metropolitan blood establishments.

When Epidemiological situation evolved on these two territories to epidemic phases at the end of January 2016, appropriate precautionary measures for blood safety have been recommended for the affected areas (Martinique, French Guiana, Guadeloupe, Saint-Martin and Saint Barthélemy), according to the recommendations of the FAG:

### For donations collected in affected areas:

- Implementation of ID ZIKA NAT testing on all blood donations collected in the affected areas for mid-February 2016 at the earlier.

### For transfused pregnant women in affected areas:

- Reserve, on priority, Red Blood Cell components collected on non-affected areas (French metropolitan areas) to pregnant women, whatever their term, when it is feasible (rare phenotypes exception).

**Table 2: Adequacy between temporary deferrals applied a priori against WNV risk and reported cases between 2010 and 2015**

Countries	Cases 2010	Adequacy 2011	Adequacy 2012	Adequacy 2013	Adequacy 2014	Strategy 2015	Adequacy 2015
Albania		2				deferred	
Algeria			1	1			1
Austria*				1	1		7
Bosnia-Herzegovina			1	3	13	deferred	
Brazil****					1	deferred	
Bulgaria**			2				2
Canada	5	101	450	108	21	deferred	78
Croatia			5	16		deferred	
Spain	2						
Greece	262	69	161	86	15	deferred	
Hungary	11	3	12	31	11	deferred	18
Israel	65	34	59	63	17	deferred	125
Italy***	2	8	50	69	24	deferred	60
Kosovo			4			deferred	
Macedonia			6	1		deferred	1
Mexico****							
Montenegro			1	4		deferred	1
Palestine	1		2		1	deferred	
Portugal							1
Romania	52	10	14	24	23	deferred	19
Russia	554	153	447	177	29	deferred	39
Serbia			70	302	76	deferred	28
Slovenia						deferred	
Tunisia		3	63	6			
Turkey	7	3	13				
Ukraine			12	1			
USA	1021	712	5674	2374	2122	deferred	2060

Green: adequate measure: a priori deferrals with reported cases OR no deferrals with no reported cases  
Red: measure applied by excess: a priori deferrals without any reported case  
Orange: measure applied during the WNV season: advisory group activation necessary  
\* 1 case in 2013 finally was cancelled  
\*\* case occurred in 2012 but reported in 2013  
\*\*\* a priori measures for regions with viral circulation last year, individual measures for other regions  
\*\*\*\* for transplant only

## SUMMARY

The advisory group allows to react quickly to emerging epidemiological alerts and to inform all institutions which are involved in transfusion safety while benefiting from a predefined strategy which can be fine-tuned every year.

Authors are acknowledging all advisory group members for their continuous involvement and their prompt and efficient cooperation.