Methods & Materials: Soldiers in the Belgian Defence are intradermally vaccinated for rabies pre-deployment since 2008 by a four injection schedule (day 0,7, 28, 365). Neutralizing antibody titers against rabies were tested 7 days after booster vaccination. Serology results of subjects, vaccinated between the 1st of april 2008 and the 31st of june 2013, were evaluated. A titer of the Rapid Fluorescent Focus Inhibition Test (RFFIT) ≥ 0,5 IU/ml is considered to be boostable. A titer > 3,0 IU/ml is considered to give sufficient protection and > 10 IU/ml a long-lasting immunity.

Results: 6598 subjects started pre-exposure rabies vaccination in the Belgian Army in these period. 1658 subjects were excluded due to lack of certainty of intradermal injection method 4940 subjects started intradermal rabies vaccination 4285 finished initial vaccination (d0, 7, 28) 1363 had a fourth vaccination (booster) 881 had a serology test (RFFIT) done after booster vaccination Median age was 36.4 year (with a standard deviation of 9,2), Gender was in 96.1% male. Neutralizing Antibodies were as follows: - 100% (881) of subjects had RFFIT above 0,5 IU/ml; - 83,3% (734) of subjects had a long-lasting immunity whit RFFIT above 10 IU/ml; - 96.6% (851) of subjects had a RFFIT above 3.0 IU/ml. We observed a delay in days of serology testing (mean = 145 (SD 6,3/range 7–1603).

Conclusion: The Classical (day 0, 7, 28, 365) Intradermal Pre-exposure Vaccination is Immunogenic and Very Promising to tackle the problem of Volume Shortage in Biologicals worldwide. Neutralizing Antibodies after four intradermal rabies injections are considered to be boostable in 100% of cases and protective in 96,6% of subjects in this largest cohort of intradermal vaccination worldwide.

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Progress towards elimination of rubella and congenital rubella syndrome in Singapore: Are we there yet?

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Background: Singapore has a comprehensive national childhood immunization programme which includes rubella. The objectives of this study were to describe the epidemiology of rubella in Singapore from 2003 to 2012, and assess its progress in implementing key control strategies against the disease, measured against the targets set by the World Health Organization (WHO) Western Pacific Regional Office (WPRO) of reducing rubella and congenital rubella syndrome (CRS) incidence to below 10 indigenous cases per million population and 10 cases per million live-births, respectively, by 2015.

Methods & Materials: Epidemiological data on all suspected and laboratory-confirmed rubella cases notified to the Ministry of Health for the period 2003-2012 were used. Data on vaccination coverage was obtained from the National Immunization Registry. To assess population immunity against rubella, two National Seroprevalence Surveys (NSS) were conducted based on residual blood samples of adult residents from the National Health Surveys in 2004 and 2010.

Results: The incidence of rubella ranged from 12–37 per million population during the 10-year period. The age-specific incidence rate of rubella was the highest in children below 5 years of age. The incidence of indigenous cases decreased from 36.2 in 2008 to 10.7 per million population in 2012. The susceptibility to rubella in women aged18-44 years decreased significantly from 15.8% in 2004 to 11.0% in 2010 (p = 0.001). Non-residents constituted 51% of the cases notified among women in this reproductive age group. There were nine cases of CRS reported during this period, and over 66% were imported cases. In the past decade, the annual vaccination coverage against measles, mumps and rubella (MMR) among Singapore residents at 2 years of age and students aged 11-12 years had been maintained between 93% and 96%. For school entrants aged 6-7 years and those aged 11 years, the annual coverage rate was between 92% and 95% from 2008 to 2012.

Conclusion: Singapore has made progress and is on track towards elimination of rubella and CRS. The NCIP has been successful in increasing the population immunity against rubella and preventing CRS through concerted efforts. The current high vaccination coverage and vigilant case surveillance should be sustained.

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Synthetic hexasaccharide of the capsular polysaccharide of *S. pneumoniae* type 14 induces cytokines

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Background: Cytokines play a crucial role in immune response. The influence of synthetic oligosaccharides on the cytokine production is not completely investigated. Aim. The study of the cytokine production in mice in response to a conjugate of a synthetic hexasaccharide fragment of the capsular polysaccharide of *S.pneumoniae* type 14 and BSA as a model protein carrier.

Methods & Materials: The hexasaccharide-BSA conjugate (HC) was prepared by the squarate method and contained, according to the MALDI-TOF data, 18 hexasaccharide residues on average. Sera from mice after immunization with HC were tested in flow cytometry using test system FlowCytomixMouse Thl/Th2 10plex (BenderMedSystems). The subisotypes of IgG were determined in ELISA using HC as a well-coating antigen. The protective activity of HC was evaluated by challenge of the immunized mice with *S. pneumoniae* type 14.

Results: Intraperitoneal injection of HC adsorbed on alum hydroxide in CBA mice led to appearance of IL-1β, IL-5, IL-6, IL-10, IL-17, TNFα, GM-CSF that increased in 2 hours and remained at the same level within 24 hours as compared with control mice. Bichromatic increase in concentration of IFNγ began to rise later - 4 h after

HC administration, and reached the maximal value (19.2 pg/ml) at the end of 24 hours considerably exceeding that in the control group (3 pg/ml). Therefore, after immunization with HC, leukocytes produced Th1, Th2 and Th17 cytokines, which play the different role in the immune response regulation. The obtained data explain the predominant production, in mice immunized with HC, of IgG1 and IgG2a subisotypes to the capsular polysaccharide of *S. pneumoniae* 14, which are connected with IL-5 and IFNγ production respectively. IL-17 produced by $CD4^+IL17^+$ stimulates the protection from extracellular bacteria including *S. pneumoniae* that was proved by challenging immunized mice with a lethal dose of *S. pneumoniae* type 14. As a result, all immunized mice survived as compared with 10% survival in the control group.

Conclusion: The ability of the hexasaccharide conjugate to stimulate production of Th1, Th2 and Th17 cytokines with the following production of IgG antibodies to the capsular polysaccharide explains its protective activity in mice after challenge with *S.pneumoniae* type 14.

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Comparison of immunogenicity elicited by two prime-boost strategies against tuberculosis

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Background: Tuberculosis remains a major health problem worldwide, and the efficacy of the only available vaccine Bacille Calmette-Guérin (BCG) varies from 0% to 80%. It is extremelyurgentto find new vaccine candidates and develop novel vaccine approaches. The disease is caused by *Mycobacterium tuberculosis* whose preferred habitat is the host macrophage, and cellular immune responses are important in against intracellular bacterial infection. An efficacious tuberculosis (TB) vaccine will probably need to induce both CD4 + and CD8 + T-cell responses specific to a protective *Mycobacterium tuberculosis* antigen(s). The gene Rv1769 has been lost from BCG-Pasteur1173 in vitro subculture, and some studies have demonstrated that it is excellent T cell antigen. To evaluate its immunogenicity, we used the prime-boost strategy to immunize BALB/c mice and detected its cellular immune response.

Methods & Materials: In our research, we immunized 4-5 week old pathogen-free BALB/c male mice by DNA/DNA and DNA/protein prime-boost vaccination strategies. Mice were killed 4, 8, 12, 16 weeks after the last boost, and we detected antibody titers in the serum, the proliferation rate of splenocytes, percentage of $CD4^+$ and $CD8^+$ T cells in the splenocytes and the IFN-γ and IL-4 levels in special antigen-stimulated splenocyte cultures to measure its immunogenicity. Measurement of these data are expressed as the mean ± standard errors(S.E.). Differences among the groups were analyzed by one-way ANOVA and differences between two groups were analyzed by Post Hoc Test and the differences were considered statistically significant for $P < 0.05$.

Results: Our data suggests that our novel DNA/DNA using Rv1769 vaccine could elicit the most long-lasting and strongest Th1 type cellular immune responses involving $CD4^+$ and $CD8^+$ T cells. This response is characterized by a strong antibody response, the proliferation rate of splenocytes, a high percentage of $CD4^+$ and $CD8^+$ T cells and high levels of IFN-γ in antigen-stimulated splenocyte cultures.

Conclusion: Our results provide evidence that the gene Rv1769 is a potential antigen or subunit vaccine to TB for further study, and in the future, we would consider build an in vivo challenge model to extend our findings to an infection/disease protection system.

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Optimal approaches for the use of DTP-HepB-Hib vaccines in Uniject™ in resource-poor settings

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Background: We evaluated the feasibility and acceptability of a new presentation of liquid DTP-HepB-Hib vaccine in a Uniject™ device in Senegal and Vietnam.

Methods & Materials: We conducted 306 interviews, nine focus group sessions, observations of immunization sessions (using injection into an orange), and a desk review of national programmatic documents. Interviews were conducted with health workers, professional representatives, and caretakers. We assessed the logistical impact of Uniject™ with the WHO-developed immunization logistics planning tool.

Results: Interviewees emphasized efficacy and safety as key factors for acceptability of a new device and most perceived that the Uniject™ device represented an improvement over existing vaccine presentations. Compared to current presentations, Uniject™ reduced vaccine waste weight and volume, including the number of empty vials (from 51% in Vietnam to 68% in Senegal). By bundling needles and syringes, Uniject™ reduced the potential for stockouts of one or the other. Time per vaccinated child decreased by 27%-61% depending on the setting.Each country used more than one DTP-HepB-Hib vaccine presentation, and Uniject™ decreased overall cold chain requirements for most but not all of these presentations. Informants reported that Uniject's™ relatively light weight compared to traditional auto-disabled syringes should facilitate both outreach and mobile strategies. Challenges also were identified. As a novel injection device, some stakeholders may require reassurance that Uniject™ represents contextually appropriate technology. Vaccinator training will be required to address several technical issues (e.g., activating the device and the motion required for vaccine delivery) and perceptions (e.g., that the plastic reservoir might freeze more easily and be difficult to handle). A key concern was that the Uniject™ device was used already in Senegal for con-