Health Academy

Radboudumc

Examination	:	**B2RQ7 Research Q7**
Date	:	April 11th 2018
Start	:	13:00 h

Your are allowed to use a calculator of the type Casio FX-82MS.

The questions must be answered in English. If you cannot remember a specific English term, you can use the Dutch term.

After finishing the exam, you can take this examination set along with you.
Please hand in the OTHER part (the answering form) to the supervisor.

During the exam you have access on a computer to these books:

- Casarett & Doull's Essentials of Toxicology (3e)

GENERAL INSTRUCTIONS:

- This exam consists of **8** open questions.
- The available time is **2** hours.
- You are allowed to use scrap paper that will be handed out. Do not use the scrap paper for your answers and do not hand it over to the supervisor.
- Check if your examination set is complete.
- Please write *your name and student number* on each page of the answering form.
- Write your answers on the answering form in the open space below the questions. Read the questions carefully before phrasing your answers.
- Be concise and complete in your answers.
- If necessary you can also use the *backside* of the pages.
- Refrain from using abbreviations in your answers, and write legibly (illegible answers are considered incorrect).
- Please do not use a pencil.
- The use of audiovisual and technical devices is not allowed, unless it is mentioned explicitly elsewhere on this page. Any inappropriate use of such equipment is regarded as fraud.
- Except for the exam forms, some loose writing material, your student and registration card your table should be empty. No boxes or cases are allowed.
- **After finishing the exam, please hand the answering form to the supervisor. If you have comments about the questions we refer you to the hyperlink of the digital comment form that is included in your "studenten webdossier" below "toetsen".**

SUCCESS!

ATTENTION !!

FIRST PUT YOUR NAME AND STUDENT NUMBER ON EVERY PAGE OF THE ANSWERING FORM!

Name: **Studentnummer:** | | | | | | | |

General question

Question 1 (10 pts)

The Health Council provides advice to the government regarding public health matters. This involves complex decision making based on factual and normative (un)certainties. The text below, which is taken from the work programme of 2018, describes a request for advice from the Minister of Health and Welfare and Sports.

Organ donation following euthanasia: protocol for determining death

In recent years there has been an increase in the number of organ donations following euthanasia in the Netherlands. This development requires a responsible combination of two procedures, namely the procedure for euthanasia and the procedure for postmortal organ donation. At the request of the Minister of Health and Welfare and Sport a working group of the Dutch Transplant Foundation has drawn up an initial version of a guideline on how that combination procedure can be implemented with maximum care and safeguards. In this context there is a need for a specific protocol to determine death. The Health Council did not consider this issue in the advisory report entitled 'Determining death in postmortal organ donation' (2015/13(R)). The Minister has now submitted an explicit request for advice to the Council so that a legal basis can be created.

The table below allows the classification of such a request based on certainty pertaining normative criteria and the knowledge about the underlying health issue.

	HIGH certainty on knowledge	LOW certainty on knowledge
HIGH consensus on normative criteria	A	B
LOW consensus on normative criteria	C	D

Which cell (A, B, C or D) of this table provides the best classification of the issue of determining death in the context of organ donation after euthanasia? (4 pts)

Explain your answer with one argument regarding the certainty of knowledge and one argument regarding the consensus on normative criteria surrounding this issue. (6 pts)

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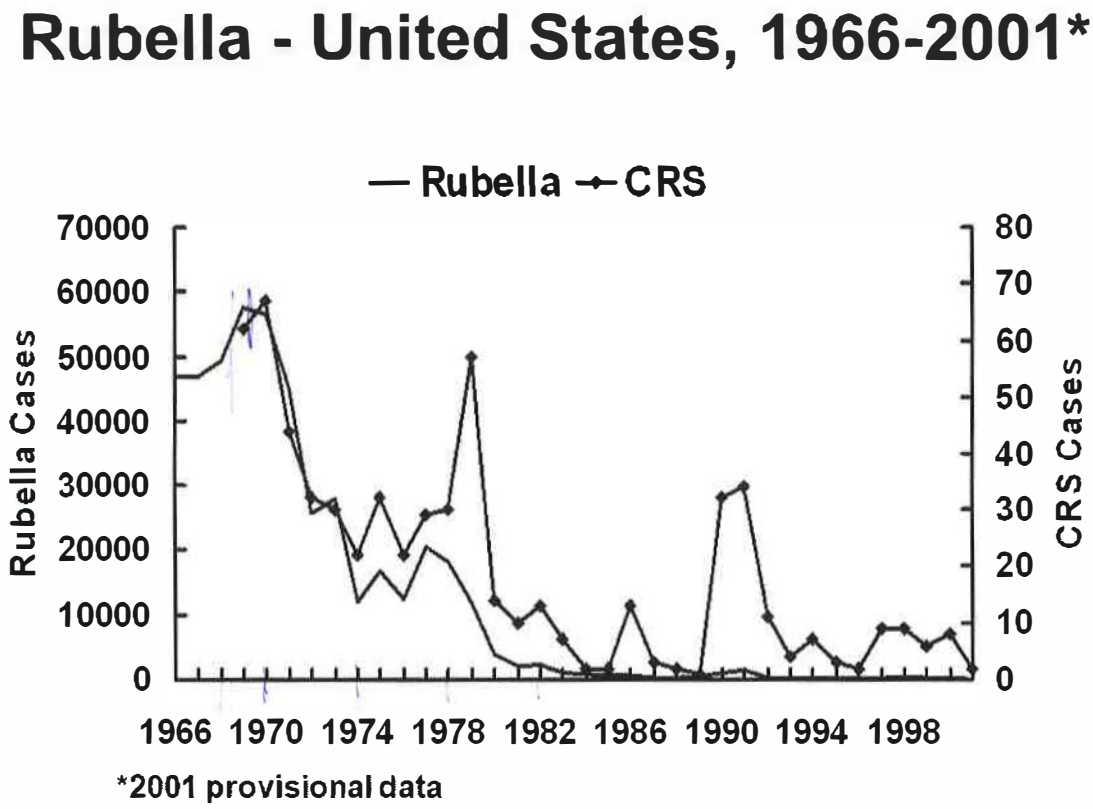
Question 3 (10 pts)

Rubella is a mild childhood disease. Humans are the only host. The virus is transmitted by the respiratory route and replicates in the nasal tissue. The biggest problem is that infection during early pregnancy may cause death of the fetus or Congenital Rubella Syndrome, with severe birth defects in eyes, heart and brain. The critical vaccine coverage for Rubella is 84%.



a. In the figure above you see the incidence in Rubella and Congenital Rubella syndrome (CRS) in the United States. After Rubella vaccination started in 1969 in the United States, a significant decrease in the incidence of Rubella was seen. Explain why an increase in congenital rubella syndrome can be seen if the critical vaccine coverage is not reached. (4 pts)

Question 4 (10 pts)

A correlate of protection is not established thus far for may vaccines and diseases, but knowing these would have major advantages.

a. Explain what is meant by a correlate of protection. (3 pts)

b. Name an advantage of the use of a correlate of protection when testing a vaccine and explain how this can be used. (3 pts)

c. Describe how a correlate of protection can be established for a vaccine in human use. (4 pts)

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Question 6 (15 points)

Formaldehyde in anatomy pathology

Formaldehyde is a small molecule (CH_2O) with strong irritating and sensitizing properties. It is used in 3-4 % dilutions in water (formalin), as fixative and preservative in anatomy and pathology departments of hospitals and universities. Exposure to formaldehyde can lead to respiratory and skin sensitization. A suggested mechanism for the observed cytogenetic damage is related to genotoxicity, including the formation of protein and DNA crosslinks. There is sufficient evidence for carcinogenicity of nasal tissues but for tumors of internal organs, more specifically of the hematological malignancies (leukemia's), the evidence is rated as 'limited' by the WHO. Overall, formaldehyde is classified as a carcinogen to humans. The available human data are not sufficient to make a reliable judgement on the reproductive toxicity of formaldehyde exposures.

a. Which three general approaches can be applied to characterize the exposure to formaldehyde? (3 pts)

b. What are the two most important sources of uncertainty in a quantitative risk assessment for reproduction toxic endpoints? (3 pts)

c. Which factors will determine the risk during anatomy classes? Provide three environmental factors and three host factors. (6pts)

d. Based on the information provided, how would you describe the *hazard* of formaldehyde in a communication to the students who follow anatomy classes involving formaline-immersed preparations? Use 2-3 short sentences. (3 points)

Name: **Studentnummer:**

Question 8 (16 points)

One of the diseases that is NOT included in the newborn screening in the Netherlands is Duchenne muscular dystrophy (DMD), a progressive X-linked neuromuscular disorder. It has an estimated worldwide incidence of 1:3500 male births. Currently, there are no curative treatments and the mean age of diagnosis is 5 years. Mothers often are pregnant again before the diagnosis of DMD in the newborn. In Wales, United Kingdom, a screening programme was introduced in 1990. Newborn bloodspots were collected routinely as part of the Wales newborn screening programme. During a 21-year period, 343,170 children were screened using a bloodspot creatine kinase (CK) assay. A total of 145 cases had a raised CK activity (Z250 U/l). The final diagnosis after a positive screening test was made after 6–8 weeks of follow-up. 79 cases had a normal serum CK, indicating absence of DMD, while 66 cases had an elevated serum CK, leading to a diagnosis of DMD by genotyping or muscle biopsy studies. This long-term study has so far identified 13 cases of DMD that had a negative CK assay.

a. What is the programme sensitivity, specificity, predictive value of a positive test (PV+), and the detection rate? Please write also down how you calculated the measures.(10 pts)

PV+ = 46 %

b. Discuss one advantage and one disadvantage of including DMD screening in the newborn screening. (4 pts)

c. The incidence of DMD in Wales was 1:5136 during the period that DMD testing was included in the NBS screening programme. Before DMD screening was included in the newborn screening programme in Wales it was 1:4046. Give an explanation for this drop in incidence. (2 pts)